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(54) Title: DETERMINING CANCER-LINKED GENES AND THERAPEUTIC TARGETS USING MOLECULAR CYTOGE-**NETIC METHODS**

548 (57) Abstract: Methods for identifying potential therapeutic agents, such as anti-tumor agents, based on their modulation of the expression of specified genes, especially genes mapping to specific chromosomal regions, are disclosed. Also described are methods for diagnosing cancerous, or potentially cancerous, conditions as a result of the expression, or patterns of expression, of such genes for diagnosing cancerous, or potentially cancerous, conditions as a result of the expression, or patterns of expression, of such genes, including detecting changes in levels of gene copy number and/or level of amplification of the said gene, or sets of genes, to detect and/or diagnose the cancer. Methods for detecting or determining functionally related genes, as well as methods for treating cancer based on targeting expression products of such genes, determining genes involved in the cancerous process and the success and/or response rates and survival statistics for cancer patients on treatment are encompassed by the invention. Also encompassed are methods involving determining the modulated expression of the genes in these regions of interest (ROIs) as pharmacodynamic/pharmacogenetic/surrogate markers and/or for patient profiling prior to accrual for clinical trials/treatments based on the identification of these genes as validated gene/drug targets in various cancer tissue types.



THERAPEUTIC TARGETS USING MOLECULAR CYTOGENETIC METHODS

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This application claims priority of U.S. Provisional Application Serial No. 60/462,895, filed 15 April 2003, the disclosure of which is hereby incorporated by reference in its entirety.

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FIELD OF THE INVENTION

The present invention relates to identification of genes whose disruption and/or change in expression is useful to distinguish cancerous from non-cancerous tissue and serve as potential therapeutic targets, pharmacodynamic /pharmacogenetic/surrogate and prognostic and diagnostic markers, and which genes are identified by high resolution Comparative Genomic Hybridization (CGH) and Spectral Karyotyping (SKY)/fluorescent *in situ* hybridization (FISH) analysis of DNA and chromosomes of various cancer cell lines and primary and metastatic tumor samples combined with gene expression analysis of these cells and tissues.

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BACKGROUND OF THE INVENTION

Chromosomal abnormalities have been identified in most cancer cells. Conventional chromosome banding techniques allow for the detection of specific chromosomal defects in tumor cells but interpretation of the banding pattern is sometimes difficult, particularly when complex chromosomal

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rearrangements or subtle abnormalities are present. In recent years, new techniques, such as CGH and SKY, based on fluorescent *in situ* hybridization (FISH) (Pinkel et al., Proc Nat Acad Sci USA 85:9138-42 (1988)) have been developed to overcome the limitations of conventional chromosome banding. CGH measures intensities of fluorescently labeled tumor DNA and normal DNA following hybridization to normal chromosomes (Kallioniemi et al., Science 258:818-21 (1992)). Gain or loss of copy number of a particular chromosome or chromosome region in the tumor DNA is determined by the relative intensity of a fluorescence ratio. SKY utilizes a cocktail of chromosome probes, fluorescently labeled to specify each chromosome, which is hybridized to tumor chromosomes in an effort to identify numerical and structural abnormalities in the tumor cell (Schröck et al., Science 273:494-7 (1996)). CGH and SKY have been used to identify chromosomal regions that harbor genes significant to the process of tumor initiation or progression.

BRIEF SUMMARY OF THE INVENTION

In one aspect the present invention relates to a set of genes that have been localized within human chromosomal regions of interest (ROI) that have been identified by molecular cytogenetic techniques.

In one aspect, the present invention relates to a method for diagnosing cancer in a mammal, especially a human patient, comprising determining amplification of a gene in the genome of a mammal wherein said gene is a gene of Table 1.

In a preferred embodiment thereof, the cancer is a member selected from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

In another preferred embodiment thereof, 3. The method of claim 1 wherein said gene of Table 1 is a gene that encodes the same gene product as a polynucleotide selected from the polynucleotides of SEQ ID NO: 1-805 and 855-923.

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In another embodiment, the present invention relates to a method for diagnosing cancer or a pre-cancerous condition in a mammal, comprising:

- (a) obtaining a cell or tissue sample from a mammal, especially a human patient, suspected of having cancer or a pre-cancerous condition and determining for said sample the gene copy number of a gene of Table 1;
- (b) comparing said gene copy number of step (a) to the gene copy number of the same gene from a sample of a corresponding cell or tissue from a mammal of the same species not having cancer of the type being diagnosed

whereby a higher gene copy number determined in step (a) relative to that in step (b) indicates the presence of a cancer or pre-cancerous condition in the mammal of step (a) and results in a diagnosis of cancer or a pre-cancerous condition in said mammal.

In a preferred embodiment of the methods of the invention, said molecule is a member selected from an antisense DNA, an antisense RNA, a ribozyme and an siRNA.

In another embodiment, the present invention relates to a method for identifying an agent having therapeutic activity in a human patient in need of said therapeutic activity, comprising:

- (a) determining in a sample from a patient the level of a gene product encoded by a gene of Table 1 prior to administering a test compound to said patient;
 - (b) administering said test compound to said patient;
- (c) determining in a sample from said patient the level of a gene product encoded by the same the gene as in step (a)

wherein a decrease in the level of said gene product in step (c) relative to step (a) identifies said test compound as an agent having therapeutic activity.

In a further embodiment, the present invention relates to a method for identifying an antineoplastic agent, comprising:

- (a) contacting a test compound with a cell that expresses a gene of Table 1; and
- (b) determining a change in gene expression as a result of said 10 contacting;

whereby said change in said gene expression identifies said test compound as an antineoplastic agent.

The present invention also relates to a method for determining the cancerous status of a cell, comprising determining elevated expression in said cell of a gene of Table 1 wherein elevated expression of said gene indicates that said cell is cancerous.

In an additional embodiment, the present invention relates to a method for identifying a compound as an anti-neoplastic agent, comprising:

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- (a) contacting a test compound with a polypeptide encoded by a gene of Table 1,
- (b) determining a change in a biological activity of said polypeptide due to said contacting,
- wherein a change in activity identifies said test compound as an agent having antineoplastic activity.

In a preferred embodiment of the foregoing, the polypeptide is an enzyme selected from kinase, protease, peptidase, phosphodiesterase, phosphatase, dehydrogenase, reductase, carboxylase. transferase, deacetylase and polymerase.

The present invention also relates to a method for identifying an antineoplastic agent comprising contacting a cancerous cell with a compound found to have anti-neoplastic activity in other the methods of the invention under conditions promoting the growth of said cell and detecting a change in the activity of said cancerous cell.

The present invention further relates to a method for treating cancer comprising contacting a cancerous cell with an agent having affinity for an expression product of a gene of Table 1 and in an amount effective to cause a reduction in cancerous activity of said cell.

The present invention also contemplates a method for monitoring the progress of cancer therapy in a patient comprising monitoring in a patient undergoing cancer therapy the expression of a gene of Table 1.

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In addition, the present invention encompasses a method for determining the likelihood of success of cancer therapy in a patient, comprising monitoring in a patient undergoing cancer therapy the expression of a gene of Table 1 wherein a decrease in said expression prior to completion of said cancer therapy is indicative of a likelihood of success of said cancer therapy.

In another embodiment, the present invention relates to a method for producing test data with respect to the anti-neoplastic activity of a compound comprising:

- (a) identifying a test compound as having anti-neoplastic activity using other methods of the invention;
- (b) producing test data with respect to the anti-neoplastic activity of said test compound sufficient to identify the chemical structure of said test compound.

Additionally, the present invention encompasses a method for determining the progress of a treatment for cancer in a patient afflicted therewith, following commencement of a cancer treatment on said patient, comprising:

- (a) determining in said patient a change in expression of one or more genes of Table 1; and
- (b) determining a change in expression of said gene compared to expression of said one or more determined genes prior to said cancer treatment;

wherein said change in expression indicates progress of said treatment thereby determining the progress of said treatment.

SEQUENCE LISTING ON CD-ROM ONLY

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The sequences disclosed herein as SEQ ID NO: 1-923 in the sequence listing are contained on compact disc (CD-ROM) only, which accompanies this application and the contents of said CD-ROMs are hereby incorporated by reference in their entirety. These sequence numbers also appear in Table 1 where all sequences are referred to as consecutive serial numbers for reference purposes only.

DETAILED SUMMARY OF THE INVENTION

The present invention relates to a set of genes that are amplified

and/or over-expressed genes in cancer cell lines and have been localized to various chromosomal regions of interest. These genes have been identified through a combination of CGH, SKY, expression analysis and Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR). Such genes are both markers and potential therapeutic targets for cancer, in particular breast.

colon, lung and prostate malignancies. In addition, the amplified nature of such genes provides a means of diagnosing a cancerous condition, or predisposition to a cancerous conditions, by determining the amplification of one or more of such genes in a patient afflicted with, or predisposed toward, or otherwise at risk of developing, cancer.

In accordance with the present invention, a number of genes have been localized to a chromosomal regions of interest as identified in Table 1 (serial number 1-229 (breast), 230-440 (colon), 441-656 (lung) and 657-805 (prostate), serial number 806-923 (transcript or protein)). The invention also includes any subsets of these. As described herein, these sequences include DNA sequences of SEQ ID NO: 1 – 805, transcripts with the sequences of SEQ ID NO: 855 – 923, and proteins/polypeptides with amino acid sequences of SEQ ID NO: 806 - 854.

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Briefly, the procedures used to identify the genes disclosed herein may be summarized as follows:

For CGH analysis, based on detailed molecular cytogenetic characterizations, the following data sets are generated, which may include regions reported in the public domain as well as unique regions not previously known.

- 1. A map of chromosomal regions involved in consistent, recurrent and high level genomic gains (i.e., amplifications) for a representative cancer cell line or tumor type (e.g. colon, prostate, breast and lung) that can be recognized as a pattern/signature for a given tumor type.
- 2. A map of chromosomal regions containing genomic losses (i.e., deletions) in each tumor type and individual cell line to be examined.
- Levels of intensities of gains and losses categorized for entry into a database.

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4. A comparison of the patterns of gains and losses between the clinical samples (e.g. colon xenografts) and cell lines (e.g., colon) of matched Stages and Grades.

5. A comparison of the patterns of gains and losses between primary prostate tumor cell lines (e.g., CPDR lines) and metastatic prostate tumor cell lines (e.g., DU 145, PC3 and LNCaP).

In accordance with the present invention, for SKY analysis, data sets were generated according to the following steps:

- Identification and development of a database of novel chromosomal rearrangements in epithelial cancer cell lines.
 - 2. Identification of novel translocations involving specific chromosomes or chromosomal regions
- Reconciliation of SKY and CGH analysis on the same cell line as a verification of the combined findings.

Combining genomic DNA analysis of gains and losses in the tumor cell lines/clinical samples with cDNA expression analysis from matched tumor types displayed on a genome template from the Golden Path genome browser using a Spotfire™ analysis tool:

- A pattern of gene expression on a U-95 Affymatix chip set obtained via the Gene Logic database was used to generate differential gene expression profiles between samples sets containing normal and malignant tissues from colon, prostate, lung, breast and various cell lines.
- 2. A Spotfire™ visualization tool was developed that allowed the generation of a list of all the genes that are present in the Golden Path within the clustered regions of gains/losses for each cell type/tumor type to generate the gene sets to include in the HITS platform
- 3. The following algorithm was employed:

i) Match chromosomal regions of amplification/gains defined by CGH with the location of genes/ESTs on an Affymatix chip as mapped to a Golden Path genome template.

- ii) Identify genes/ESTs over-expressed in tumor tissue compared to normal tissue in said chromosomal regions using the Gene Logic database.
- iii) Compile data on cell lines of a particular tumor type and different tumor types showing clusters of genomic gains and losses at certain chromosomal regions.
- iv) Pick BACs that span the chromosomal regions consistently gained and containing over-expressed genes in an effort to positionally clone novel cancer genes (oncogenes and genes in relevant pathways)
- Validate the identified genes by
 A) Picking STS markers that identify the gene sequence and quantify the relative copy number in genomic DNA and RNA across a panel of tumor cell lines.
 - B) Develop probes for FISH on chromosomes from tumor cell lines and primary tumor tissue micro-arrays.

4. The expression data from tumor cell lines that have undergone SKY/CGH analysis was used to pick candidate genes to validate as individual targets in functional genomic assays and in-vivo assays and for use in the transcriptional assay platform.

In accordance with the present invention, over-expression of cellular genes is conveniently monitored in model cellular systems using cell lines (such as is used in the example below), primary cells, or tissue samples maintained in growth media. For different purposes, these may be treated with compounds at one or more different concentrations to assay for modulating agents. Thus, cellular RNAs were isolated from the cells or cultures as an indicator of selected gene expression. The cellular RNAs were then divided

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and subjected to analysis that detected the presence and/or quantity of specific RNA transcripts, which transcripts were then amplified for detection purposes using standard methodologies, such as reverse transcriptase polymerase chain reaction (RT-PCR). The levels of specific RNA transcripts, including their presence or absence, were determined. When used for identification of modulating agents, such as anti-neoplastic agents, a metric is derived for the type and degree of response of the treated sample compared to control samples.

In accordance with the foregoing, the genes identified as being amplified and/or over-expressed, which can include increased copy number thereof, in cancerous cells are localized in chromosomal regions of interest as identified in Table 1 (serial number 1-229 (breast), 230-440 (colon), 441-656 (lung) and 657-805 (prostate); for polypeptide SEQ ID NOs, see Table 1, serial number 806-923 (transcript or protein)).

These genes may be utilized to characterize, the cancerous, or non-cancerous, status of cells, or tissues. The methods of the invention may be used with a variety of cell lines or with primary samples from tumors maintained *in vitro* under suitable culture conditions for varying periods of time, or *in situ* in suitable animal models.

The genes disclosed herein are expressed at levels in cancer cells that are different from the expression levels in non-cancer cells. These genes as identified in Table 1 are amplified in cancer cells relative to non-cancer cells of corresponding tissues, especially breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

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In accordance with the foregoing, the present invention relates to a method for diagnosing cancer in a mammal, comprising determining amplification of a gene in the genome of a mammal wherein said gene is a gene of Table 1.

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In a preferred embodiment thereof, said gene of Table 1 is a gene that encodes the same gene product as a polynucleotide selected from the polynucleotides of SEQ ID NO: 1 – 805 and 855 - 923. In a further preferred embodiment, said mammal is a human patient.

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The present invention is also directed to a method for diagnosing cancer or a pre-cancerous condition in a mammal, preferably a human patient, comprising:

- (a) obtaining a cell or tissue sample from a mammal suspected of
 having cancer or a pre-cancerous condition and determining for said sample
 the gene copy number of a gene of Table 1;
 - (b) comparing said gene copy number of step (a) to the gene copy number of the same gene from a sample of a corresponding cell or tissue from a mammal of the same species not having cancer of the type being diagnosed

whereby a higher gene copy number determined in step (a) relative to that in step (b) indicates the presence of a cancer or pre-cancerous condition in the mammal of step (a) and results in a diagnosis of cancer or a pre-cancerous condition in said mammal.

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In specific embodiments, the cancer to be diagnosed is one or more of breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

Preferably, the gene of Table 1 is a gene that encodes the same gene product as a polynucleotide of SEQ ID NO: 1 – 805 and 855– 923.

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The present invention is also directed to a method of inhibiting cancer, or a pre-cancerous condition, in a mammalian cell, comprising contacting said cell with a molecule that inhibits function of a gene of Table 1. Preferably, the gene of Table 1 is a gene that encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 - 923. In a specific embodiment thereof, said molecule inhibits gene function by binding to said gene. In other embodiments, the molecule inhibits gene function by binding to an RNA encoded by said gene or inhibits gene function by binding to polypeptide encoded by said gene. Preferably, the molecule is a member selected from an antisense DNA, an antisense RNA, a ribozyme and an siRNA. Also preferred is where the cancer is a member selected from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

The invention contemplates that such contacting occurs in vivo.

The invention also relates to a method for identifying an agent having therapeutic activity in a human patient in need of said therapeutic activity, comprising:

- (a) determining in a sample from a patient the level of a gene product encoded by a gene of Table 1 prior to administering a test compound to said patient;
 - (b) administering said test compound to said patient:
- (c) determining in a sample from said patient the level of a gene product encoded by the same the gene as in step (a)

wherein a decrease in the level of said gene product in step (c) relative to step (a) identifies said test compound as an agent having therapeutic activity.

Preferably, said therapeutic activity is anticancer activity and said cancer is one or more of breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

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Also preferred is where said gene product is an RNA or a polypeptide, especially where an activity of the polypeptide is determined, preferably an enzyme activity. In specific embodiments, said gene of Table 1 is a gene that encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 – 923, as well as where said molecule is a member selected from an antisense DNA, an antisense RNA, a ribozyme and an siRNA.

The present invention also relates to a method for identifying an antineoplastic agent, comprising:

- (a) contacting a test compound with a cell that expresses a gene of Table 1; and
- (b) determining a change in gene expression as a result of said contacting;

whereby said change in said gene expression identifies said test compound as an antineoplastic agent.

Most preferred is where the change in expression is a decrease in expression. The contacting may occur *in vivo*. Also preferred is where said gene of Table 1 encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 – 923 and where said molecule is a member selected from an antisense DNA, an antisense RNA, ribozyme, an siRNA, a small organic molecule and an antibody.

The present invention also relates to a method for determining the cancerous status of a cell, comprising determining elevated expression in said cell of a gene of Table 1 wherein elevated expression of said gene indicates that said cell is cancerous. Preferably, wherein said elevated expression is an elevated copy number of the gene and wherein said gene of Table 1 encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 - 923.

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The present invention further relates to a method for identifying a compound as an anti-neoplastic agent, comprising:

(a) contacting a test compound with a polypeptide encoded by a gene of Table 1.

(b) determining a change in a biological activity of said polypeptide due to said contacting,

wherein a change in activity identifies said test compound as an agent having antineoplastic activity.

Preferably, said gene of Table encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 - 923.

In a preferred embodiment, the change in biological activity is a decrease in biological activity.

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In another preferred embodiment, the biological activity is an enzyme activity, such as where the enzyme is one selected from the group kinase, protease, peptidase, phosphodiesterase, phosphatase, dehydrogenase, reductase, carboxylase. transferase, deacetylase and polymerase.

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Assays for these available. enzymes are such for as phosphodiesterases (the pharmacologically most relevant phosphodiesterases are those that hydrolyze cyclic nucleotides (see, for example, cAMP and cGMP assays available from Perkin-Elmer, as well as Estrade et al., Eur. J. Pharmacol. 352:2-3, 157-163 (1998)).

Protein phosphatases remove phosphate residues from proteins. Most tests of their activity use the same assays as for protein kinases. A non-radioactive phosphatase assay system is available from Promega Biotech.

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The therapeutically most relevant dehydrogenases oxidize or reduce small molecular weight metabolites, esp. steroid hormones, or that generally use or generate NAD or NADP (see: Haeseleer et al., J. Biol. Chem., 273:21790-21799 (1998)). A commercial assay is available from Cayman Chemical (at www.caymanchem.com).

Gamma-carboxylases are important enzymes in the blood coagulation process. The main assay protocols use synthetic peptides (see: Ulrich et al., J. Biol. Chem., 263:9697-9702 (1988); Begley et al., J. Biol. Chem., 275:36245-36249 (2000)).

In highly preferred embodiments, the kinase is one of a protein kinase, a serine or threonine kinase, or a receptor tyrosine protein kinase. Where the polypeptide encoded by a gene of the invention is a protein kinase, especially involving tyrosine kinase, various assays for activity are available. Protein kinases add phosphate groups to serine, threonine or tyrosine residues on proteins, most commonly measured with phospho-serine, threonine, or tyrosine-specific antibodies, or generation of radiolabeled substrate, or consumption of ATP, or phosphorylation of (synthetic) small peptides, or measuring downstream enzyme activity and gene transcription. Such assays are commercially available. (See, for example, the tyrosine kinase assay from Roche Molecular Biochemicals). Assays for serine/threonine kinases are also available at Chromagen.com, Upstate Biotechnology, Inc. (Lake Placid, NY, and at upstatebiotech.com) and from Applied BioSystems (Foster City, CA (home.appliedbiosystems.com)).

In other specific embodiments, the protease is a serine protease, cysteine protease or aspartic acid protease, or the transferase is a methyltransferase, preferably a cytosine methyltransferase or an adenine methyltransferase, or the deacetylase is a histone deacetylase, or the

carboxylase is a γ -carboxylase, or the peptidase is a zinc peptidase, or the polymerase is a DNA polymerase or an RNA polymerase.

Proteases degrade proteins, un-specifically or at specific sites. Almost all pharmacologically relevant ones have very narrowly defined specific substrates, and their activity is most often measured by directly measuring cleavage product or generation of (fluorescent) light after cleavage of synthetic substrates. Assays are available for serine proteases (Calbiochem, Palo Alto, CA, and see Berdichevsky et al., J. Virol. Methods, 107:245-255 (2003), for systeine proteases (See: Schulz et al., Mol. Pathol., 51:222-24 (1998) and Selzer et al., PNAS, 96:11015-11022 (1999)), for aspartic acid proteases (Geno Tech, Inc. at www.genotech.com) and for zinc peptidases (see Evans et al., J. Biol. Chem., 278:23180-23186 (2003)).

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Both (regulatory) DNA-methylases and (biosynthetic) protein methylases that are drug targets. (See: Jonassen and Clarke, J. Biol. Chem., 275:12381-12387 (2000); Jackson et al., Nature, 416:556-560 (2002)).

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Most HDAC (histone deacetylase) assays use colorimetric or fluorometric (synthetic) substrates. Standard assays are for binding, especially molecular size changes, blocking a specific site, and effects on transcription or downstream reactions (if DNA or RNA is the direct target of a drug). A commercial assay is available from Vinci Biochem (at www.vincibiochem.it).

In another specific embodiment, the biological activity is a membrane transport activity, preferably wherein the polypeptide is a cation channel protein, an anion channel protein, a gated-ion channel protein or an ABC

transporter protein. Drug effects on the activity of transporter and channel proteins are screened by measuring increase or decrease of the ((radio-)labeled) transported entity inside or outside the cell, in cell-based assays, ATP consumption (in the case of ATPases), or changes in cell membrane potential. Assays employing such proteins are available, such as for ABC transporter (see: Marcil et al., Lancet, 354:1341-46 (1999) and for ion channels (from Evotec OAI, at www.evotecoai.com and from PharmaLinks, at www.pharmalinks.org/research/cellsignalling).

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In one embodiment, the polypeptide is an integrin (the signal transduction pathways elicited by the integrins are slow and not very well characterized, hence most assays are either just binding assays or measure downstream biological phenomena (such as migration, invasion, etc.) (See: Ganta et al., Endocrinology, 138:3606-3612 (1997); Sim et al., J. Biomed. Mater. Research, 68A:352-359 (2004); and Weinreb et al., Anal. Biochem., 306:305-313 (2002)), or a Cytochrome P450 enzyme (almost all cytochrome assays require knowledge of what the substrate is and measure conversion of substrate (free or (radio-)labeled) or generation of product; useful C¹⁴-labeled substrates are available from Amersham Biosciences at www1.amershambiosciences.com), or a nuclear hormone receptor (Assays available from Discoverx, Fremont, CA, such as an estrogen assay; also see Rosen et al., Curr. Opin. Drug. Discov. Devel., 6:224-30 (2003)).

In one preferred embodiment, the biological activity is a receptor activity, preferably where the receptor is a G-protein-coupled receptor (GPCR).

GPCRs are transmembrane proteins that wind 7 times back and forth through a cell's plasma membrane with a ligand binding site located on the outside of the membrane surface of the cell and the effector site

being present inside the cell. These receptors bind GDP and GTP. In response to ligand binding, GPCRs activate signal transduction pathways which induce a number of assayable physiological changes, e.g., an increase in intracellular calcium levels, cyclic-AMP, inositol phosphate turnover, and downstream gene transcription (directly or via reporterassays) along with other translocation assays available for measuring GPCR activation when the polypeptide encoded by a gene of the invention is a GPCR. Thus, such proteins work through a second messenger. The result is activation of CREB, a transcription factor that stimulates the production of gene products. One useful assay is the so-called BRET2/arrestin assay, useful in screening for compounds that interact with GPCRs. (See: Bertrand et al, J. Recept. Signal Transduct Res., 22:533-41 (Feb.-Nov. 2002)). In addition, numerous assays are commercially available, such as the Transfluor Assay, available from Norak Biosciences, Inc. (www.norakbio.com) or ArrayScan and KineticScan, both from Cellomics, or assays from CyBio (Jena, Germany).

Assays useful with the invention are usually set up to screen for agonists or antagonists after adding ligand, but effects on most of these parameters can be measured whether or not the ligand for the receptor is known. Such assays may involve radioligand-binding assays. Activation of the majority of GPCRs by agonists leads to the interaction of beta-arrestin (a protein that is involved in receptor desensitization and sequestration) with the receptor, which is measurable by fluorescence energy transfer

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The disclosure of all journal articles, or other publications, referred to herein are hereby incorporated by reference in their entirety.

In one embodiment, the polypeptide is in a solution or suspension and contact with the test compound is by direct contact between the test compound and the protein molecule. Alternatively, the polypeptide may be in

a cell and the test compound may have to diffuse into the cell in order to contact the polypeptide. In an alternative embodiment, the test compound may be contacted with a cell that contains or expresses the polypeptide but the test compound may have no direct contact with the polypeptide. In stead, the test compound may act to induce production and/or activity of a different compound, such as an intracellular second messenger that serves to contact the polypeptide and modulate or change the biological activity of this polypeptide.

In accordance with the foregoing, the method of the present invention includes cancer modulating agents that are themselves either polypeptides, or small chemical entities, that affect the cancerous process, including initiation, suppression or facilitation of tumor growth, either *in vivo* or *ex vivo*. Such agents may also be antibodies that react with one or more polypeptides encoded by genes as disclosed herein, preferably polypeptides comprising any one of the amino acid sequences of SEQ ID NO: 806 – 854.

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Because the genes disclosed herein are over-expressed and relate to the cancerous condition of a cell, successful anti-neoplastic activity will commonly be exhibited by agents that reduce the expression of said genes as identified in Table 1. In one embodiment thereof, the change in expression is a decrease in copy number of the gene or genes under study. In accordance therewith, said change in gene copy number is conveniently determined by detecting a change in expression of messenger RNA encoded by said gene sequence. In another preferred embodiment, expression is determined for more than one such gene, such as 2, 5, 10 or more of the genes.

Other methods useful in measuring a change in expression of the genes disclosed herein include measuring a change in the amount or rate of synthesis of a polypeptide encoded by said gene, preferably a decrease in synthesis of said polypeptide. Most preferably, the polypeptide comprises an

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amino acid sequence highly homologous to a sequence for genes as identified in Table 1 (SEQ ID NO: 1 - 923).

The methods of the invention can thus be utilized to identify antineoplastic agents useful in treatment of cancerous conditions. Such activity can be further modified by first identifying such an agent using an assay as already described and further contacting such agent with a cancerous cell, followed by monitoring of the status of said cell, or cells. A change in status indicative of successful anti-neoplastic activity may include a decrease in the rate of replication of the cancerous cell(s), a decrease in the total number of progeny cells that can be produced by said cancerous cell(s), or a decrease in the number of times said cancerous cell(s) can replicate, or the death of said cancerous cell(s).

Anti-neoplastic agents may also be identified using recombinant cells suitably engineered to contain and express the cancer-related genes disclosed herein. In one such embodiment, a recombinant cell is formed using standard technology and then utilized in the assays disclosed herein. Methods of forming such recombinant cells are well known in the literature. See, for example, Sambrook, et al., Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor, N.Y., (1989), Wu et al, *Methods in Gene Biotechnology* (CRC Press, New York, NY, 1997), and *Recombinant Gene Expression Protocols*, in *Methods in Molecular Biology*, Vol. 62, (Tuan, ed., Humana Press, Totowa, NJ, 1997), the disclosures of which are hereby incorporated by reference.

The present invention also relates to a method for detecting the cancerous status of a cell, comprising detecting elevated copy number and/or expression in said cell of at least one gene that maps to the chromosomal region of interest as identified in Table 1 (SEQ ID NO: 1 – 923). Such elevated expression may be readily monitored by comparison to that of otherwise normal cells having the same genes. Elevated expression of these

genes is indicative of the cancerous state. This includes a gene corresponding to a polynucleotide that comprises a nucleotide sequence as identified in Table 1 (SEQ ID NO: 1 — 923). Such elevated expression, including increased copy number, may be the expression of more than one such gene.

The present invention also relates to a method for detecting a cancer-linked gene comprising the steps of contacting a compound identified as having gene modulating activity for a gene corresponding to a polynucleotide that comprises a nucleotide sequence as identified in Table 1 (SEQ ID NO: 1 – 923) with a cell expressing a test gene and detecting modulation, such as decreased activity, of such test gene relative to when said compound is not present thereby identifying said test gene as a cancer-related gene. In preferred embodiments, the gene determined by said method is an oncogene, or cancer facilitating gene.

In another embodiment, there is provided a method for treating cancer comprising contacting a cancerous cell with an agent first identified as having gene modulating activity using any of the assay methods disclosed according to the invention and in an amount effective to reduce the cancerous activity of said cell. In a preferred embodiment, the cancerous cell is contacted *in vivo*. In other preferred embodiments, said reduction in cancerous activity is a decrease in the rate of proliferation of said cancerous cell, or said reduction in cancerous activity is the death of said cancerous cell.

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The present invention further relates to a method for treating cancer comprising contacting a cancerous cell with an agent having activity against an expression product encoded by a gene corresponding to a polynucleotide comprising a nucleotide sequence as identified in Table 1 (SEQ ID NO: 1 – 923)where the product is a polypeptide, most preferably one comprising an amino acid sequence as identified in Table 1 (SEQ ID NO: 806 - 854). In a

preferred embodiment, said cancerous cell is contacted in vivo. In another preferred embodiment, the agent is an antibody.

As noted, the genes useful in the assay methods include genes mapping within chromosomal regions of interest and genes as identified in Table 1 (SEQ ID NO: 1-923), or a gene that encodes the same RNA, such as the same messenger RNA, whose corresponding cDNA is one of the sequences as identified in Table 1 (SEQ ID NO: 1-923). The genes useful in the methods of the invention further include genes encoding RNAs whose corresponding cDNA is at least 90% identical to a sequence as identified in Table 1 (SEQ ID NO: 1-923), preferably at least about 95% identical to such a sequence, more preferably at least about 98% identical to such sequence and most preferably one comprising that sequence are specifically contemplated by all of the methods of the present invention.

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In addition, sequences encoding the same proteins (SEQ ID NO: 806 – 854) as any of these sequences, regardless of the percent identity of such sequences, are also specifically contemplated by the invention.

The sequences disclosed herein may be genomic in nature and thus represent the sequence of an actual gene, such as a human gene, or may be a cDNA sequence derived from a messenger RNA (mRNA) and thus represent contiguous exonic sequences derived from a corresponding genomic sequence or they may be wholly synthetic in origin for purposes of testing. As described in the Example, the expression of these cancer-related genes is determined from the relative expression levels of the RNA complement of a cancerous cell relative to a normal (i.e., non-cancerous) cell. Because of the processing that may take place in transforming the initial RNA transcript into the final mRNA, the sequences disclosed herein may represent less than the full genomic sequence. They may also represent sequences derived from ribosomal and transfer RNAs. Consequently, the genes present in the cell (and representing the genomic sequences) and the sequences

disclosed herein, which are mostly cDNA sequences, may be identical or may be such that the cDNAs contain less than the full genomic sequence. Such genes and cDNA sequences are still considered corresponding sequences because they both encode similar RNA sequences. Thus, by way of non-limiting example only, a gene that encodes an RNA transcript, which is then processed into a shorter mRNA, is deemed to encode both such RNAs and therefore encodes an RNA complementary to (using the usual Watson-Crick complementarity rules), or that would otherwise be encoded by, a cDNA (for example, a sequence as disclosed herein). Thus, the sequences disclosed herein correspond to genes contained in the cancerous or normal cells used to determine relative levels of expression because they represent the same sequences or are complementary to RNAs encoded by these genes. Such genes also include different alleles and splice variants that may occur in the cells used in the methods of the invention.

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The genes of the invention "correspond to" a polynucleotide having a sequence as identified in Table 1 (SEQ ID NO: 1 - 923) if the gene encodes an RNA (processed or unprocessed, including naturally occurring splice variants and alleles) that is at least 90% identical, preferably at least 95% identical, most preferably at least 98% identical to, and especially identical to, an RNA that would be encoded by, or be complementary to, such as by hybridization with, a polynucleotide having the indicated sequence. In addition, genes including sequences at least 90% identical to a sequence as identified in Table 1 (SEQ ID NO: 1 - 923), preferably at least about 95% identical to such a sequence, more preferably at least about 98% identical to such sequence and most preferably comprising such sequence are specifically contemplated by all of the methods of the present invention as being genes that correspond to these sequences. In addition, sequences encoding the same proteins as any of these sequences, regardless of the percent identity of such sequences, are also specifically contemplated by any of the methods of the present invention that rely on any or all of said sequences, regardless of how they are otherwise described or limited. Thus,

any such sequences are available for use in carrying out any of the methods disclosed according to the invention. Such sequences also include any open reading frames, as defined herein, present within any of the sequences as identified in Table 1 (SEQ ID NO: 1-805 and 855-923).

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Further in accordance with the present invention, the term "percent identity" or "percent identical," when referring to a sequence, means that a sequence is compared to a claimed or described sequence after alignment of the sequence to be compared (the "Compared Sequence") with the described or claimed sequence (the "Reference Sequence"). The Percent Identity is then determined according to the following formula:

Percent Identity = 100 [1-(C/R)]

wherein C is the number of differences between the Reference Sequence and the Compared Sequence over the length of alignment between the Reference Sequence and the Compared Sequence wherein (i) each base or amino acid in the Reference Sequence that does not have a corresponding aligned base or amino acid in the Compared Sequence and (ii) each gap in the Reference Sequence and (iii) each aligned base or amino acid in the Reference Sequence that is different from an aligned base or amino acid in the Compared Sequence, constitutes a difference; and R is the number of bases or amino acids in the Reference Sequence over the length of the alignment with the Compared Sequence with any gap created in the Reference Sequence also being counted as a base or amino acid.

If an alignment exists between the Compared Sequence and the Reference Sequence for which the percent identity as calculated above is about equal to or greater than a specified minimum Percent Identity then the Compared Sequence has the specified minimum percent identity to the Reference Sequence even though alignments may exist in which the

hereinabove calculated Percent Identity is less than the specified Percent Identity.

As used herein, the terms "portion," "segment," and "fragment," when used in relation to polypeptides, refer to a continuous sequence of residues, such as amino acid residues, which sequence forms a subset of a larger sequence. For example, if a polypeptide were subjected to treatment with any of the common endopeptidases, such as trypsin or chymotrypsin, the oligopeptides resulting from such treatment would represent portions, segments or fragments of the starting polypeptide. When used in relation to a polynucleotide, such terms refer to the products produced by treatment of said polynucleotides with any of the common endonucleases, or any stretch of polynucleotides that could be synthetically synthesized.

As used herein, the term "DNA segment" or "DNA sequence" refers to a DNA polymer, in the form of a separate fragment or as a component of a larger DNA construct, which has been derived from DNA, and may include both single stranded and duplex sequences. Such segments are provided in the form of an open reading frame uninterrupted by internal non-translated sequences, or introns, which are typically present in eukaryotic genes.

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The term "coding region" refers to that portion of a gene which either naturally or normally codes for the expression product of that gene in its natural genomic environment, i.e., the region coding *in vivo* for the native expression product of the gene.

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The term "nucleotide sequence" refers to a heteropolymer of deoxyribonucleotides. Generally, DNA segments encoding the proteins provided by this invention are assembled from cDNA fragments and short oligonucleotide linkers, or from a series of oligonucleotides, to provide a synthetic gene which is capable of being expressed in a recombinant transcriptional unit comprising regulatory elements derived from a microbial or viral operon.

The term "expression product" means that polypeptide or protein that is the natural translation product of the gene and any nucleic acid sequence coding equivalents resulting from genetic code degeneracy and thus coding for the same amino acid(s).

The term "fragment," when referring to a coding sequence, means a portion of DNA comprising less than the complete coding region whose expression product retains essentially the same biological function or activity as the expression product of the complete coding region.

The present invention also finds use as a means of diagnosing the presence of cancer in a patient, as where a sample of cancerous tissues or cells, or tissues or cells suspected of being cancerous. For such purposes, and in accordance with the disclosure elsewhere herein, such diagnosis is based on the detection of elevated expression or amplification, such as elevated copy number, of one or more of the genes identified according to the invention. Such elevated expression can be determined by any of the means described herein.

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In one such embodiment, the elevated expression, as compared to normal cells and/or tissues of the same organ, is determined by measuring the relative rates of transcription of RNA, such as by production of corresponding cDNAs and then analyzing the resulting DNA using probes developed from the gene sequences as identified in Table 1. Thus, the levels of cDNA produced by use of reverse transcriptase with the full RNA complement of a cell suspected of being cancerous produces a corresponding amount of cDNA that can then be amplified using polymerase chain reaction, or some other means, such as rolling circle amplification, to determine the relative levels of resulting cDNA and, thereby, the relative levels of gene expression.

For RNA analysis, the latter may be isolated from samples in a variety of ways, including lysis and denaturation with a phenolic solution containing a chaotropic agent (e.g., triazol) followed by isopropanol precipitation, ethanol wash, and resuspension in aqueous solution; or lysis and denaturation followed by isolation on solid support, such as a Qiagen resin and reconstitution in aqueous solution; or lysis and denaturation in non-phenolic, aqueous solutions followed by enzymatic conversion of RNA to DNA template copies. Steady state RNA levels for a given type of cell or tissue may have to be ascertained prior to employment of the methods of the invention but such is well within the skill of those in the art and will not be further described in detail herein.

Alternatively, increased expression, such as increased copy number, may be determined for the genes present in a cancerous cell, or a cell suspected of being cancerous, by using the nucleotides sequences as identified in Table 1 as a means of generating probes for the DNAs present in the cells to be examined. Thus, the DNA of such cells may be extracted and probed using the sequences disclosed herein for the presence in the genomes of such cells of increased amounts of one or more of the genes of the invention. For example, where a cancer-related, or cancer-linked, gene as disclosed herein is found to be present in multiple copies within the genome of a cell, even where it may not be actively being over-expressed at the time of such determination, this may be indicative of at least a disposition toward developing cancer at a subsequent time.

In accordance with the foregoing, the presence of such multiple copies of a gene, or genes, as disclosed herein may be determined using northern or southern blotting and employing the sequences as identified in Table 1 to develop probes for this purpose. Such probes may be composed of DNA or RNA and may advantageously be comprised of a contiguous stretch of nucleotide residues matching, or complementary to, a sequence as identified in Table 1. Such probes will most usefully comprise a contiguous stretch of at

least 15, preferably at least 30, more preferably at least 50, most preferably at least 80, and especially at least 100, even 200 residues, derived from one or more of the sequences as identified in Table 1. Thus, where a single probe binds multiple times to the genome of a sample of cells that are cancerous, or are suspected of being cancerous, or predisposed to become cancerous, whereas binding of the same probe to a similar amount of DNA derived from the genome of otherwise non-cancerous cells of the same organ or tissue results in observably less binding, this is indicative of the presence of multiple copies of a gene comprising, or corresponding to, the sequence as identified in Table 1 from which the probe sequenced was derived.

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Increased expression may also be determined using agents that selectively bind to, and thereby detect, the presence of expression products of the genes disclosed herein. For example, an antibody, possibly a suitably labeled antibody, such as where the antibody is bound to a fluorescent or radiolabel, may be generated against one of the polypeptides comprising a sequence as identified in Table 1 (serial number 1-229 (breast), 230-440 (colon), 441-656 (lung) and 657-805 (prostate); for polypeptide SEQ ID NOs, see Table 1, serial number 806-923 (transcript or protein)), and said antibody will then react with, binding either selectively or specifically, to a polypeptide encoded by one of the genes that corresponds to a sequence disclosed herein. Such antibody binding, especially relative extent of such binding in samples derived from suspected cancerous, as opposed to otherwise noncancerous, cells and tissues, can then be used as a measure of the extent of expression, or over-expression, of the cancer-related genes identified herein. Thus, the genes identified herein as being over-expressed in cancerous cells and tissues may be over-expressed due to increased copy number, or due to over-transcription, such as where the over-expression is due to overproduction of a transcription factor that activates the gene and leads to repeated binding of RNA polymerase, thereby generating large than normal amounts of RNA transcripts, which are subsequently translated into polypeptides, such as the polypeptides comprising amino acid sequences as

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identified in Table 1 (SEQ ID NO: 1 - 923). Such analysis provides an additional means of ascertaining the expression of the genes identified according to the invention and thereby determining the presence of a cancerous state in a sample derived from a patient to be tested, of the predisposition to develop cancer at a subsequent time in said patient.

In employing the methods of the invention, it should be borne in mind that gene expression indicative of a cancerous state need not be characteristic of every cell found to be cancerous. Thus, the methods disclosed herein are useful for detecting the presence of a cancerous condition within a tissue where less than all cells exhibit the complete pattern of over-expression. For example, a set of selected genes, comprising sequences homologous under stringent conditions, or at least 90%, preferably 95%, identical to at least one of the sequences as identified in Table 1, may be found, using appropriate probes, either DNA or RNA, to be present in as little as 60% of cells derived from a sample of tumorous, or malignant, tissue while being absent from as much as 60% of cells derived from corresponding non-cancerous, or otherwise normal, tissue (and thus being present in as much as 40% of such normal tissue cells). In a preferred embodiment, such gene pattern is found to be present in at least 70% of cells drawn from a cancerous tissue and absent from at least 70% of a corresponding normal, non-cancerous, tissue sample. In an especially preferred embodiment, such gene pattern is found to be present in at least 80% of cells drawn from a cancerous tissue and absent from at least 80% of a corresponding normal, non-cancerous, tissue sample. In a most preferred embodiment, such gene pattern is found to be present in at least 90% of cells drawn from a cancerous tissue and absent from at least 90% of a corresponding normal, noncancerous, tissue sample. In an additional embodiment, such gene pattern is found to be present in at least 100% of cells drawn from a cancerous tissue and absent from at least 100% of a corresponding normal, non-cancerous, tissue sample, although the latter embodiment may represent a rare occurrence.

In an additional aspect, the present invention relates to a method for determining a cancer initiating or facilitating gene comprising contacting a cell expressing a test gene (i.e., a gene whose status as a cancer initiating or 5 facilitating gene is to be determined) with an agent that decreases the expression of a gene that encodes an RNA at least 90%, preferably 95%, identical to an RNA encoded by (i.e., a gene corresponding to) a polynucleotide comprising, or having, a sequence selected from the group consisting as identified in Table 1 and detecting a decrease in expression of said test gene compared to when said agent is not present, thereby identifying said test gene as being a cancer initiating or facilitating gene. Such genes may, of course, be oncogenes and said decrease in expression may be due to a decrease in copy number of said gene in said cell or a cell derived from said cell, such as where copy number is reduced in the cells formed by replication of such cells.

Thus, some or all of the genes disclosed herein as corresponding to as identified in Table 1 are found to play a direct role in the initiation or progression of cancer or even other diseases and disease processes. Because changes in expression of these genes (up-regulation) are linked to the disease state (i.e. cancer), the change in expression may contribute to the initiation or progression of the disease. For example, if a gene that is upregulated is an oncogene such a gene provides for a means of screening for small molecule therapeutics beyond screens based upon expression output alone. For example, genes that display up-regulation in cancer and whose elevated expression contributes to initiation or progression of disease represent targets in screens for small molecules that inhibit or block their function. Examples include, but are not be limited to, kinase inhibition, cellular proliferation, substrate analogs that block the active site of protein targets, etc.

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It should be noted that there are a variety of different contexts in which genes have been evaluated as being involved in the cancerous process.

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Thus, some genes may be oncogenes and encode proteins that are directly involved in the cancerous process and thereby promote the occurrence of cancer in an animal. Other genes may simply be involved either directly or indirectly in the cancerous process or condition and may serve in an ancillary capacity with respect to the cancerous state. All such types of genes are deemed with those to be determined in accordance with the invention as disclosed herein. Thus, the gene determined by said method of the invention may be an oncogene, or the gene determined by said method may be a cancer facilitating gene, the latter including a gene that directly or indirectly affects the cancerous process, either in the promotion of a cancerous condition or in facilitating the progress of cancerous growth or otherwise modulating the growth of cancer cells, either in vivo or ex vivo. Such genes may work indirectly where their expression alters the activity of some other gene or gene expression product that is itself directly involved in initiating or facilitating the progress of a cancerous condition. For example, a gene that encodes a polypeptide, either wild or mutant in type, which polypeptide acts to suppress of tumor suppressor gene, or its expression product, will thereby act indirectly to promote tumor growth.

In accordance with the foregoing, the method of the present invention includes cancer modulating agents that are themselves either polypeptides, or small chemical entities, that affect the cancerous process, including initiation, suppression or facilitation of tumor growth, either *in vivo* or *ex vivo*. Such agents may also be antibodies that react with one or more of the polypeptides as identified in Table 1 ((SEQ ID NO: 806-923 (transcript or protein)).

In keeping with the disclosure herein, the present invention also relates to a method for treating cancer comprising contacting a cancerous cell with an agent having activity against an expression product encoded by a gene mapping within regions of chromosomal interest or, alternatively, a gene corresponding to a polynucleotide that comprises a nucleotide sequence as

identified in Table 1, such as where such expression product is one the polypeptides as identified in Table 1.

The method of the present invention includes embodiments of the above-recited method wherein said cancer cell is contacted *in vivo* as well as *ex vivo*, preferably wherein said agent comprises a portion, or is part of an overall molecular structure, having affinity for said expression product. In one such embodiment, said portion having affinity for said expression product is an antibody.

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In one embodiment of the present invention, a chemical agent, such as a protein or other polypeptide, is joined to an agent, such as an antibody, having affinity for an expression product of a cancerous cell, such as a polypeptide or protein encoded by a gene related to the cancerous process. especially a gene sequence corresponding to one of the cDNA sequences as identified in Table 1. In a specific embodiment, said expression product acts as a therapeutic target for the affinity portion of said anticancer agent and where, after binding of the affinity portion of such agent to the expression product, the anti-cancer portion of said agent acts against said expression product so as to neutralize its effects in initiating, facilitating or promoting tumor formation and/or growth. In a separate embodiment of the present invention, binding of the agent to said expression product may, without more, have the effect of deterring cancer promotion, facilitation or growth, especially where the presence of said expression product is related, either intimately or only in an ancillary manner, to the development and growth of a tumor. Thus, where the presence of said expression product is essential to tumor initiation and/or growth, binding of said agent to said expression product will have the effect of negating said tumor promoting activity. In one such embodiment, said agent is an apoptosis-inducing agent that induces cell suicide, thereby killing the cancer cell and halting tumor growth.

Many cancers contain chromosomal rearrangements, which typically represent translocations, amplifications, or deletions of specific regions of genomic DNA. A recurrent chromosomal rearrangement that is associated with a specific stage and type of cancer always affects a gene (or possibly genes) that play a direct and critical role in the initiation or progression of the disease. Many of the known oncogenes or tumor suppressor genes that play direct roles in cancer have either been initially identified based upon their positional cloning from a recurrent chromosomal rearrangement or have been demonstrated to fall within a rearrangement subsequent to their cloning by other methods. In all cases, such genes display amplification at both the level of DNA copy number and at the level of transcriptional expression at the mRNA level.

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The present method also relates to a method for determining functionally related genes comprising contacting one or more gene sequences corresponding to the cDNAs as identified in Table 1 with an agent that modulates expression of more than one gene in such group and thereby determining a subset of genes of said group.

In accordance with the present invention, said functionally related genes are genes modulating the same metabolic pathway or said genes are genes encoding functionally related polypeptides. In one such embodiment, said genes are genes whose expression is modulated by the same transcriptional activator or enhancer sequence, especially where said transcriptional activator or enhancer increases, or otherwise modulates, the activity of a gene corresponding to a cDNA as identified in Table 1.

The present invention also relates to a process that comprises a method for producing a product comprising identifying an agent according to one of the disclosed methods for identifying such an agent (i.e., the therapeutic agents identified according to the assay procedures disclosed herein) wherein said product is the data collected with respect to said agent

as a result of said identification process, or assay, and wherein said data is sufficient to convey the chemical character and/or structure and/or properties of said agent. For example, the present invention specifically contemplates a situation whereby a user of an assay of the invention may use the assay to screen for compounds having the desired enzyme modulating activity and, having identified the compound, then conveys that information (i.e., information as to structure, dosage, etc) to another user who then utilizes the information to reproduce the agent and administer it for therapeutic or research purposes according to the invention. For example, the user of the assay (user 1) may screen a number of test compounds without knowing the structure or identity of the compounds (such as where a number of code numbers are used the first user is simply given samples labeled with said code numbers) and, after performing the screening process, using one or more assay processes of the present invention, then imparts to a second user (user 2), verbally or in writing or some equivalent fashion, sufficient information to identify the compounds having a particular modulating activity (for example, the code number with the corresponding results). This transmission of information from user 1 to user 2 is specifically contemplated by the present invention.

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In accordance with the foregoing, the present invention relates to a method for producing test data with respect to the anti-neoplastic activity of a compound comprising:

- (a) contacting a compound with a cell that expresses at least one gene corresponding to a polynucleotide comprising a nucleotide sequence of serial number 1-229 (breast), 230-440 (colon), 441-656 (lung) and 657-805 (prostate) of Table 1 or encoding a polypeptide or transcript of SEQ ID NO: 806-923 and under conditions promoting expression of said gene;
- (b) detecting a change in expression of said gene compared to expression when said compound is not present; and
 - (c) producing test data with respect to the gene modulating activity of said compound based on a change in the expression of the determined gene,

or genes, whose expression is otherwise elevated in a non-cancerous cell over that in a cancerous cell and a decrease in the expression of the determined gene, or genes whose expression is otherwise increased in a cancerous cell over that in a non-cancerous cell indicating anti-neoplastic activity.

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In another embodiment, the present invention provides a method for monitoring the progress of a cancer treatment, such as where the methods of the invention permit a determination that a given course of cancer therapy is or is not proving effective because of an increased or decreased expression of a gene, or genes, disclosed herein. For example, where there is an increased copy number of one or more of the genes as identified in Table 1 (SEQ ID NO: 1-805), monitoring of such genes can predict success or failure of a course of therapy, such as chemotherapy, or predict the likelihood of a relapse based on elevated activity or expression of one or more of these genes following such course of therapy.

In accordance with the foregoing, the present invention contemplates a method for determining the progress of a treatment for cancer in a patient afflicted with cancer, following commencement of a cancer treatment on said patient, comprising:

- (a) determining in said patient a change in expression of one or more genes corresponding to a polynucleotide comprising a nucleotide sequence of serial number 1-229 (breast), 230-440 (colon), 441-656 (lung) and 657-805 (prostate) of Table 1 or encoding a polypeptide or transcript of serial number 806-923 of Table 1 (which include any of SEQ ID NO: 1 923) and under conditions promoting expression of said one or more genes; and
- (b) detecting a change in expression of said gene compared to expression of said one or more determined genes prior to commencement of said cancer treatment;

thereby determining the progress of said treatment.

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In a preferred embodiment, the detected change in expression is a decrease in expression. In another preferred embodiment, the cancer treatment is treatment with a chemotherapeutic agent, especially an agent that modulates, preferably decreases, expression of a gene identified herein. such as where said agent was first identified as having anti-neoplastic activity using a method of the invention. Thus, in accordance with this aspect of the present invention, a patient, or even a research animal, such as a mouse, rat. rabbit or primate, afflicted with cancer, including a cancer induced for research purposes, is introduced to a cancer treatment regimen, such as administration of an anti-cancer agent, including one first identified as having anti-neoplastic activity by one or more of the screening methods disclosed herein. The progress and success or failure of such treatment is subsequently ascertained by determining the subsequent expression of one or more, preferably at least 3, or 5, or 10, of the genes identified herein, or that encodes a transcript or polypeptide disclosed herein (see Table 1) following said treatment. In a preferred embodiment, a treatment that reduces said expression is deemed advantageous and may then be the basis for continuing said treatment. The methods of the invention thereby provide a means of continually monitoring the success of the treatment and evaluating both the need, and desirability, of continuing said treatment. In addition, more than one said treatment may be administered simultaneously without diminishing the value of the methods of the invention in determining the overall success of such combined treatment. Thus, more than one said anti-neoplastic agent may be administered to the same patient and overall effectiveness ascertained by the recited methods.

In accordance with the foregoing, the present invention also contemplates a method for determining the likelihood of survival of a patient afflicted with cancer, following commencement of a cancer treatment on said patient, comprising:

(a) determining in said patient a change in expression of one or more genes corresponding to a polynucleotide comprising a nucleotide sequence of

serial number 1-229 (breast), 230-440 (colon), 441-656 (lung) and 657-805 (prostate) of Table 1 or encoding a polypeptide or transcript of serial number 806-923 of Table 1 and under conditions promoting expression of said one or more genes; and

(b) detecting a change in expression of said gene compared to expression of said one or more determined genes prior to commencement of said cancer treatment;

thereby determining the likelihood of survival of said treatment.

In a preferred embodiment, the detected change in expression is a decrease in expression and said determined gene, or genes, may include 2, 3, 5, 10 or more of the genes described herein. Thus, the methods of the invention may be utilized as a means for compiling cancer survival statistics following one or more, possibly combined, treatments for cancer as in keeping with the other methods disclosed herein.

The genes identified herein also offer themselves as pharmacodynamic markers (or as pharmacogenetic and/or surrogate markers), such as for patient profiling prior to clinical trials and/or targeted therapies, including combination treatments, resulting from the identification of these genes as valid gene targets for chemotherapy based on the screening procedures of the invention. In one embodiment thereof, the likelihood of success of a cancer treatment with a selected chemotherapeutic agent may be based on the fact that such agent has been determined to have expression modulating activity with one or more genes identified herein, especially where said genes have been identified as showing elevated expression levels in samples from a prospective patient afflicted with cancer. Methods described elsewhere herein for determining cancerous status of a cell may find ready use in such evaluations.

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It should be cautioned that, in carrying out the procedures of the present invention as disclosed herein, any reference to particular buffers,

media, reagents, cells, culture conditions and the like are not intended to be limiting, but are to be read so as to include all related materials that one of ordinary skill in the art would recognize as being of interest or value in the particular context in which that discussion is presented. For example, it is often possible to substitute one buffer system or culture medium for another and still achieve similar, if not identical, results. Those of skill in the art will have sufficient knowledge of such systems and methodologies so as to be able, without undue experimentation, to make such substitutions as will optimally serve their purposes in using the methods and procedures disclosed herein.

The present invention will now be further described by way of the following non-limiting example. In applying the disclosure of the example, it should be kept clearly in mind that other and different embodiments of the methods disclosed according to the present invention will no doubt suggest themselves to those of skill in the relevant art.

20 EXAMPLE

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Cancerous cells that over-express one or more of the genes selected from those that correspond to genes as identified in Table 1 (serial number 1-229 (breast), 230-440 (colon), 441-656 (lung) and 657-805 (prostate); serial number 806-923 (transcript or protein), or SEQ ID NO: 1 – 805 and 855 – 923) are grown to a density of 10⁵ cells/cm² in Leibovitz's L-15 medium supplemented with 2 mM L-glutamine (90%) and 10% fetal bovine serum. The cells are collected after treatment with 0.25% trypsin, 0.02% EDTA at 37°C for 2 to 5 minutes. The trypsinized cells are then diluted with 30 ml growth medium and plated at a density of 50,000 cells per well in a 96 well plate (200 μl/well). The following day, cells are treated with either compound buffer alone, or compound buffer containing a chemical agent to be tested, for 24 hours. The media is then removed, the cells lysed and the RNA recovered

using the RNAeasy reagents and protocol obtained from Qiagen. RNA is quantitated and 10 ng of sample in 1 μ l are added to 24 μ l of Taqman reaction mix containing 1X PCR buffer, RNAsin, reverse transcriptase, nucleoside triphosphates, amplitaq gold, tween 20, glycerol, bovine serum albumin (BSA) and specific PCR primers and probes for a reference gene (18S RNA) and a test gene (Gene X). Reverse transcription is then carried out at 48°C for 30 minutes. The sample is then applied to a Perlin Elmer 7700 sequence detector and heat denatured for 10 minutes at 95°C. Amplification is performed through 40 cycles using 15 seconds annealing at 60°C followed by a 60 second extension at 72°C and 30 second denaturation at 95°C. Data files are then captured and the data analyzed with the appropriate baseline windows and thresholds.

The quantitative difference between the target and reference genes is then calculated and a relative expression value determined for all of the samples used. This procedure is then repeated for each of the target genes in a given signature, or characteristic, set and the relative expression ratios for each pair of genes is determined (i.e., a ratio of expression is determined for each target gene versus each of the other genes for which expression is measured, where each gene's absolute expression is determined relative to the reference gene for each compound, or chemical agent, to be screened). The samples are then scored and ranked according to the degree of alteration of the expression profile in the treated samples relative to the control. The overall expression of the set of genes relative to the controls, as modulated by one chemical agent relative to another, is also ascertained. Chemical agents having the most effect on a given gene, or set of genes, are considered the most anti-neoplastic.

Table

Protein/ Transcript			ated	ιό.					ted					inase								ONA
Description	hypothetical protein FLJ20354 unknown	24-dehydrocholesterol reductase	kinesin-like 6 (mitotic centromere-associated	kinesin) CDC20 cell division cycle 20 homolog (S.	cerevisiae) interferon-stimulated protein 15 kDa	unknown	ESTs	immunoglobulin superfamily member 9	kinase interacting with leukemia-associated	gene (stathmin)	cell division cycle associated 1	HSPC150 protein similar to ubiquitin-	conjugating enzyme	similar to rat nuclear ubiquitous casein kinase 2	centromere protein F 350/400ka (mitosin)	centromere protein A 17kDa	ribonucleotide reductase M2 polypeptide	hypothetical protein FLJ25211	TTK protein kinase	ESTS	KIAA0906 protein	Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 1913076
unigene	Hs.133260 NULL	Hs.75616	Hs.69360	Hs.82906	Hs.833	NULL	Hs. 133294	Hs.38002	Hs.127310	!	Hs.234545	Hs.5199		Hs.118064	Hs.77204	Hs.1594	Hs.75319	Hs.44269	Hs.169840	Hs.196042	Hs.56966	Hs.41271
pand	p31.2 p31.3	p32.3	p34.1	p34.2	036.33	q21.3	d22	q23.1	q23.2		q23.3	q32.1	•	q32.1	q32.3	p23.3	p25.1	q33.1	p21.31	p24.3	p25.1	q12.3
chr		-	-	_	-	-	_	_	_	•	-	_		-	~	7	7	7	က	ო	က	ო
m_q	primary primary	primary	primary	primary	primary	primary	primary	primary	primary	•	primary	primary	•	primary	primary	primary	primary	primary	primary	primary	primary	primary
tissue	breast breast	breast	breast	breast	breast	breast	breast	breast	breast	•	breast	breast		breast	breast	breast	breast	breast	breast	breast	breast	breast
accession	AK000490 R33352	AI739473	U63743	U05340	AA203213	T16144	AI053741	AB037776	AA830844	1	AF326731	AB032931		Al380204	U30872	U14518	AI492879	AL045632	M86699	AI962335	AI867102	AI751438
SEQ	e 1	13	2	7	-	12	₹	4	O		7	4		ω	9	55	54	26	74	11	75	71
Serial No.	- 8	က	4	2	ဖ	7	ω	6	9	;	Ţ	75		13	4	15	16	17	18	1 0	20	21

collagen type VIII alpha 1 ESTs Moderately similar to zinc finger protein	91 (HPF7 HTF10) [Homo sapiens] [H.sapiens] epithelial cell transforming sequence 2	oncogene ESTs	FYN binding protein (FYB-120/130)	cyclin B1	paired-like homeodomain transcription factor 1	RAB6 interacting kinesin-like (rabkinesin6)	kinesin-like 2	inhibin beta A (activin A activin AB alpha	polypeptide)	HOMO Sapiens CUNA FLJ11041 fis cione PLACE1004405	anillin actin binding protein (scraps homolog	Drosophila)	sorting nexin 10	anterior gradient 2 homolog (Xenepus laevis)	enhancer of zeste homolog 2 (Drosophila)	solute carrier family 39 (zinc transporter)	member 4	Homo sapiens clone IMAGE:5455669 mRNA	partial cds	T-LAK cell-originated protein kinase	pituitary tumor-transforming 1	sulfatase FP	tumor protein D52	cyclin É2	mal T-cell differentiation protein 2	hypothetical protein MGC5254	squalene epoxidase
Hs.114599 Hs.36830	Hs.122579	Hs.195225	Hs.58435	Hs.23960	Hs.84136	Hs.73625	Hs.20830	Hs.727		HS.20192	Hs.62180		Hs.106260	Hs.91011	Hs.77256	Hs.352415		Hs.67776		Hs.104741	Hs.252587	Hs.70823	Hs.2384	Hs.30464	Hs.76550	Hs.222088	Hs.71465
q12.3 q26.1	q26.32	q28	p13.1	q13.2	q31.1	q31.2	p21.32	p14.1		0 4	p14.2		p15.2	p21.1	q36.1	NOLL		NOLL		p21.1	q13.2	q13.3	q21.13	q22.1	q24.12	q24.13	q24.13
က က	က	က	2	2	5	2	ဖ	7	1	•	7		7	7	7	∞		ω		ω	ω	∞	ω	∞	∞	ω	ω
primary primary	primary	primary	primary	primary	primary	primary	primary	primary	•	primary	primary	•	primary	primary	primary	primary		primary		primary	primary	primary	primary	primary	primary	primary	primary
breast breast	breast	breast	breast	breast	breast	breast	breast	breast	1	preast	breast		breast	breast	breast	breast		breast		breast	breast	breast	breast	breast	breast	breast	breast
X57527 W02608	AI823992	A1087975	AW001872	BE407516	U70370	AI739117	D14678	M13436	1040404	A154540/	AK023208		AI285531	A1922323	U61145	AA625199		AI949095		AI932328	AA203476	AW043713	BE974098	AF091433	AA046853	AI925583	AF098865
72 76	73	78	82	80	8	79	83	85	ć	8	84		83	87	88	66		100		06	91	92	96	98	92	93	26
23	24	25	56	27	28	59	30	31	ç	25	33		34	35	36	37		38		39	40	41	42	43	44	45	46

Homo sapiens cDNA FLJ14388 fis clone HEMBA1002716	zinc finger DHHC domain containing 12	hypothetical protein FLJ36779	EST	ZW10 interactor	cell division cycle 2 G1 to S and G2 to M	hypothetical protein FLJ10540	KIAA0750 gene product	similar to RIKEN cDNA 2610036L13	serologically defined colon cancer antigen 28	H2A histone family member X	Thy-1 cell surface antigen	forkhead box M1	Rac GTPase activating protein 1	cullin 4A	cyclin-dependent kinase inhibitor 3 (CDK2-	associated dual specificity phosphatase)	cyclin B2	KIAA0101 gene product	protein regulator of cytokinesis 1	tubulin beta 4	HSPC037 protein	hypothetical protein MGC4692	selenoprotein X 1	hypothetical protein MGC2605	hypothetical protein FLJ30002	hypothetical protein MGC2601	Homo sapiens similar to possible G-protein	receptor clone MGC:21993 IMAGE:4398317 mRNA complete cds	ESTS
Hs.9812	Hs.133122	Hs.212613	Hs.274152	Hs.42650	Hs.334562	Hs.14559	Hs.314434	Hs.23044	Hs.84700	Hs.147097	Hs.125359	Hs.239	Hs.23900	Hs.183874	Hs.84113		Hs.194698	Hs.81892	Hs.344037	Hs.159154	Hs.108196	Hs.13561	Hs.279623	Hs.124015	Hs.351474	Hs.124915	Hs.290943		Hs.368078
q24.22	q34.11	q34.3	q34.3	q21.1	q21.2	q23.33	p15.3	q13.1	q13.4	q23.3	q23.3	p13.33	q13.12	q33.3	q22.1		q21.3	q22.2	q25.3	NOLL	NOLL	p13.3	p13.3	p13.3	p13.3	p13.3	p13.3		q12.2
∞ .	တ	တ	တ	9	10	10	7	7	11	11	7	12	12	13	7		15	15	15	16	16	16	16	16	16	10	16		16
primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary		primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary		primary
breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast		breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast		breast
AA147884	AW007586	W25552	AI811865	AF067656	AL524035	AI674163	AB018293	AL079372	D60944	X14850	AA704137	U74612	U82984	AI291142	L25876		AL080146	D14657	AA195614	AW003626	BC003186	AI819340	W92110	AI953838	AL520675	BE965311	AI701742		AA904482
94	103	101	102	17	16	15	21	18	22	19	20	23	24	25	56		27	28	59	સ	32	30	34	35	36	37	38		33
47	48	49	20	51	52	53	54	55	26	22	58	26	09	61	62		63	2	65	99	29	89	69	20	71	72	73		74

Table 1 (Continued)

KIAA1618 protein solute carrier family 16 (monocarboxylic acid transporters) member 3	hypothetical protein BC014072 ESTs Moderately similar to TP2A_HUMAN DNA topoisomerase II alpha isozyme	In.saplensj topoisomerase (DNA) II alpha 170kDa unknown Homo sapiens Similar to epsin 3 clone MGC:1006 IMAGE:3505495 mRNA complete	cds ESTs Weakly similar to hypothetical protein FLJ20489 [Homo sapiens] [H.sapiens]	Homo sapiens cDNA FLJ36569 fis clone TRACH2010824 highly similar to	hypothetical protein MGC11138 karyopherin alpha 2 (RAG cohort 1 importin alpha 1)	hematological and neurological expressed 1 thymidine kinase 1 soluble highly expressed in cancer rich in leucine	ubjudit repeats ubiduitin UBF-fl KIAA0186 gene product retinoic acid induced 3 chromosome 20 open reading frame 1 SCAN domain containing 1 ubiquitin-conjugating enzyme E2C	ribosomal protein L4 breast carcinoma amplified sequence 4
Hs.314169 Hs.85838	Hs.348504 Hs.370428	Hs.156346 NULL Hs.307036	Hs.165909	Hs.103512	Hs.90207 Hs.159557	Hs.109706 Hs.105097 Hs.58169	Hs.288549 Hs.36232 Hs.194691 Hs.9329 Hs.274411 Hs.93002	Hs.286 Hs.56237
NULL	q11.2 q21.31	921.31 921.31 922	q23.2	q23.2	q24.2 q24.3	q25.3 q25.3 p11.32	q13.43 p11.21 p11.23 q11.12 q13.12	q13.12 q13.13
17	71	71 71	17	17	17	14 14	5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	2 2
primary primary	primary primary	primary primary primary	primary	primary	primary primary	primary primary primary	primary primary primary primary primary primary	primary primary
breast breast	breast breast	breast breast breast	breast	breast	breast breast	breast breast breast	breast breast breast breast breast	breast breast
AI683036 U81800	BE328850 AW003286	AL561834 L47276 BC001038	AA424160	BF029215	AI675178 U28386	AA635844 K02581 AF017790	AA719022 D80008 AI990405 AA534688 AW003586 U73379	A1990026 AA207074
44 44	45 39	44 48 64	40	51	43 50	46 47 52	53 57 59 59	62 67
75 76	77	79 80 81	82	83	84 85	86 87 88	89 90 90 93 93	90 90

Table 1 (Continued)

breast carcinoma amplified sequence 1	serine/threonine kinase 6	transmembrane prostate androgen induced RNA	eukarvotic translation elongation factor 1 alpha	. 2	collagen type I alpha 1	KDEL (Lys-Asp-Glu-Leu) endoplasmic	reticulum protein retention receptor 3	hypothetical protein MGC861	hypothetical protein FLJ20354	unknown	24-dehydrocholesterol reductase	kinesin-like 6 (mitotic centromere-associated	kinesin) CDC20 cell division cycle 20 homolog (S		microfibrillar-associated protein 2	interferon-stimulated protein 15 kDa	unknown	ESTs	immunoglobulin superfamily member 9	kinase interacting with leukemia-associated	gene (stathmin)	unknown	cell division cycle associated 1	ESTs	ESTs	HSPC150 protein similar to ubiquitin-	conjugating enzyme	similar to rat nuclear ubiquitous casein kiriase 2	
Hs.129057	Hs.250822	Hs.83883	Hs.2642		Hs.172928	Hs.250696		Hs.208912	Hs.133260	NULL	Hs.75616	Hs.69360	He 82906		Hs.83551	Hs.833	NOLL	Hs.133294	Hs.38002	Hs.127310		NOLL	Hs.234545	Hs.191187	Hs.209609	Hs.5199	12 440064	13. 1 10004	
q13.2	q13.31	q13.32	a13.33	-	q13.1	q13.1		q13.2	p31.2	p31.3	p32.3	p34.1	n34.2	1	p36.13	p36.33	q21.3	d22	q23.1	q23.2		q23.2	q23.3	q23.3	q25.2	q32.1	4 000	435. I	
20	70	20	20		22	22		22	~	~			~	-	_	_	~	_	_	~		-		_	<u>``</u>	₹-	7	-	
primary	primary	primary	primary		primary	primary	•	primary	metastatic	metastatic	metastatic	metastatic	metactatic		metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	6;10;00;00	metastatic	
breast	breast	breast	breast		breast	breast		breast	breast	breast	breast	breast	hreact		breast	breast	breast	breast	breast	breast		breast	breast	breast	breast	breast	400	Dieasi	
AF041260	AF011468	AA535819	X70940		Y15915	AL035081		AI381686	AK000490	R33352	AI739473	U63743	1105340		A1992172	AA203213	T16144	AI053741	AB037776	AA830844		R62346	AF326731	AI983896	AI798144	A1990409	**************************************	A1300204	
09	61	28	9		69	20		89	106	113	116	108	105	2	119	114	115	104	118	112		120	110	117	121	107	7	=	
26	86	66	100) }	101	102		103	104	105	106	107	40 80 10 80	3	109	110	111	112	113	114		115	116	117	118	119	5	120	

Table 1 (Continued)

centromere protein F 350/400ka (mitosin) centromere protein A 17kDa	ribonucleotide reductase M2 polypeptide	hypothetical protein FLJ25211	hairy and enhancer of split 6 (Drosophila)	TTK protein kinase	unknown	ESTs	KIAA0906 protein	Homo sapiens mRNA full length insert cDNA	clone EUROIMAGE 1913076	collagen type VIII alpha 1	ESTs Moderately similar to zinc finger protein	91 (HPF7 HTF10) [Homo sapiens] [H.sapiens]	ESTs	epithelial cell transforming sequence 2	oncogene	ESTS	FYN binding protein (FYB-120/130)	cyclin B1	paired-like homeodomain transcription factor 1	RAB6 interacting kinesin-like (rabkinesin6)	kinesin-like 2	inhibin beta A (activin A activin AB alpha	polypeptide)	Homo sapiens cDNA FLJ11041 fis clone	PLACE1004405	anillin actin binding protein (scraps homolog Drosophila)	Homo sapiens Similar to RIKEN cDNA E130201N16 gene clone IMAGE:3845782	mRNA
Hs.77204 Hs.1594	Hs.75319	Hs.44269	Hs.42949	Hs.169840	NULL	Hs.196042	Hs.56966	Hs.41271		Hs.114599	Hs.36830		Hs.128773	Hs.122579		Hs.195225	Hs.58435	Hs.23960	Hs.84136	Hs.73625	Hs.20830	Hs.727		Hs.28792	,	Hs.62180	Hs.91109	
q32.3 p23.3	p25.1	q33.1	q37.3	p21.31	p21.31	p24.3	p25.1	q12.3		q12.3	q26.1		q26.31	q26.32		d28	p13.1	q13.2	q31.1	q31.2	p21.32	p14.1		p14.1	,	p14.2	p15.1	
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metastatic metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic		metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	•	metastatic	metastatic	
breast breast	breast	breast	breast	breast	breast	breast	breast	breast		breast	breast		breast	breast		breast	breast	breast	breast	breast	breast	breast		breast	•	breast	breast	
U30872 U14518	AI492879	AL045632	N21131	M86699	AA663786	AI962335	AB020713	AI557210		X57527	W02608		AI760298	AI823992		AI087975	AW001872	N90191	U70370	AI739117	D14678	M13436		AA059458		AK023208	AI742239	
109	168	170	171	191	197	194	195	188		189	192		193	190		196	201	199	200	198	202	204	,	205	0	203	211	
121	123	124	125	126	127	128	129	130		131	132		133	134		135	136	137	138	139	140	141	!	142	(143	144	

Table 1 (Continued)

sorting nexin 10 anterior gradient 2 homolog (Xenepus laevis) collagen type I alpha 2 polymerase (RNA) II (DNA directed)	enhancer of zeste homolog 2 (Drosophila) solute carrier family 39 (zinc transporter) member 4	Homo sapiens clone IMAGE:5455669 mRNA partial cds	kinesin family member C2-like	rhophilin 1	T-LAK cell-originated protein kinase pituitary tumor-transforming 1	sulfatase FP	tumor protein D52	cyclin E2	ESTS	mai T-ceil differentiation protein 2	hypothetical protein MGC5254	squalene epoxidase	Homo sapiens cDNA FLJ14388 its clone HEMBA1002716	zinc finger DHHC domain containing 12	hypothetical protein FLJ36779	EST	ZW10 interactor	cell division cycle 2 G1 to 5 and G2 to M	hypothetical protein FLJ10540	_	Homo sapiens cDINA r L332323 ils ciorie
Hs.106260 Hs.91011 Hs.179573 Hs.80475	Hs.77256 Hs.352415	Hs.67776	Hs.92679	Hs.149152	Hs.104741 Hs 252587	Hs.70823	Hs.2384	Hs.30464	Hs.162697	Hs.76550	Hs.222088	Hs.71465	Hs.9812	Hs.133122	Hs.212613	Hs.274152	- Hs.42650	Hs.334562	Hs.14559	HS.88/8	Hs.185918
p15.2 p21.1 q21.3 q22.1	936.1 NULL	NULL	NOL P	NOLL	p21.1	q13.2 q13.3	q21.13	q22.1	q24.11	q24.12	q24.13	q24.13	q24.22	q34.11	q34.3	q34.3	q21.1	q21.2	q23.33	q23.33	p15.1
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breast breast breast breast	breast breast	breast	breast breast	breast	breast	breast breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast
AI285531 AI922323 AI961907 L37127	U61145 AA625199	AI949095	W22510 AA292431	AI917311	A1932328	AA2034/6 RE500977	BE974098	AF091433	AA610522	AA046853	AI656807	D78130	AA147884	AW007586	W25552	AI811865	AF067656	D88357	AI674163	<b>U37426</b>	AA705015
208 206 209 210	207 220	223	224 225	226	212	213 215	217	219	222	216	218	221	214	229	227	228	124	123	122	125	131
145 146 147	149	151	152 153	54	52	56	28	59	160	161	162	163	164	165	166	167	168	169	170	171	172

SMINT2000060	KIAA0750 gene product similar to RIKEN cDNA 2610036L13	serologically defined colon cancer antigen 28	H2A histone family member X	Thy-1 cell surface antigen	forkhead box M1	Rac GTPase activating protein 1	Human clone 295 5cM region surrounding	hepatocyte nuclear tactor-1a/MODY3 mKNA	cullin 4A	cyclin-dependent kinase inhibitor 3 (CDK2-	associated dual specificity phosphatase)	cyclin B2	KIAA0101 gene product	protein regulator of cytokinesis 1	tubulin beta 4	HSPC037 protein	Homo sapiens cDNA FLJ14059 fis clone	HEMBB1000573	ESTs Highly similar to hypothetical protein	rtaloos (nomo sapiens) kimothotiol antoin MOCARO	nypotnetical protein MGC4682	seienoprotein A 1	hypothetical protein MGC2605	hypothetical protein FLJ30002	hypothetical protein MGC2601	Homo sapiens similar to possible G-protein recentor clone MGC:21993 IMAGE:4398317	mRNA complete cds	serine/arginine repetitive matrix 2	ESTs
	Hs.314434 Hs.23044	Hs.84700	Hs.147097	Hs.125359	Hs.239	Hs.23900	Hs.204166		Hs.183874	Hs.84113		Hs.194698	Hs.81892	Hs.344037	Hs.159154	Hs.108196	Hs.289047		Hs.115838	110 40564	HS.13301	HS.21.9023	Hs.124015	Hs.351474	Hs.124915	Hs.290943		Hs.197114	Hs.368078
	p15.3	q13.4	q23.3	q23.3	p13.33	q13.12	q24.31		q33.3	q22.1		q21.3	q22.2	q25.3	NULL	NULL	p12.3	•	p12.3	4	0.0 0.0	p13.3	p13.3	p13.3	p13.3	p13.3		p13.3	q12.2
	<del>+ + + + + + + + + + + + + + + + + + + </del>	=======================================	7	7	12	7	12	,	73	14		15	15	15	9	16	16		16	ć	9 9	9	9	16	16	10		16	16
	metastatic metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	•	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic
	breast breast	breast	breast	breast	breast	breast	breast		breast	breast		breast	breast	breast	breast	breast	breast		breast	1	Dreast	preast	breast	breast	breast	breast		breast	breast
	AB018293	AF151810	X14850	AA704137	U74612	U82984	R61322		AI291142	L25876		AL080146	D14657	AA195614	AW003626	BC003186	AI766311		AI344053	070	AI819340	W92110	A1953838	AL520675	BE965311	AI701742		AI655799	AA904482
	129	130	127	128	132	133	134		135	136		137	138	139	141	142	149		151	,	140	144	145	146	147	148		150	143
	173	175	176	177	178	179	180		181	182		183	184	185	186	187	188		189	0	180 180	191	192	193	194	195		196	197

Table 1 (Continued)

KIAA1618 protein solute carrier family 16 (monocarboxylic acid transporters) member 3	hypothetical protein BC014072 ESTs Moderately similar to TP2A_HUMAN DNA topoisomerase II alpha isozyme [H.sapiens]	topoisomerase (DNA) II alpha 170kDa unknown	Homo sapiens Similar to epsin 3 clone MGC:1006 IMAGE:3505495 mRNA complete	ESTs Weakly similar to hypothetical protein FLJ20489 [Homo sapiens]	Homo sapiens cDNA FLJ36569 fis clone TRACH2010824 highly similar to	hypothetical protein MGC11138	karyopherin alpha 2 (RAG cohort 1 importin	ESTS	thymidine kinase 1 soluble	hematological and neurological expressed 1	highly expressed in cancer rich in leucine heptad repeats	ubiquitin UBF-fl	KIAA0186 gene product	retinoic acid induced 3	chromosome 20 open reading frame 1	SCAN domain containing 1	ubiquitin-conjugating enzyme E2C	ribosomal protein L4
Hs.314169 Hs.85838	Hs.348504 Hs.370428	Hs.156346 NULL	Hs.307036	Hs.165909	Hs.103512	Hs.90207	Hs.159557	Hs.42645	Hs.105097	Hs.109706	Hs.58169	Hs.288549	Hs.36232	Hs.194691	Hs.9329	Hs.274411	Hs.93002	Hs.286
NULL	q11.2 q21.31	q21.31 q21.31	d22	q23.2	q23.2	d24.2	q24.3	q24.3	q25.3	q25.3	p11.32	q13.43	p11.21	p11.23	q11.1	q11.22	q13.12	q13.12
17	17	17	17	17	17	17	1	17	17	17	18	19	20	20	20	20	20	20
metastatic metastatic	metastatic metastatic	metastatic metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic
breast breast	breast breast	breast	breast	breast	breast	hreact	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast
AI683036 U81800	BE328850 AW003286	AI375913	BC001038	AA424160	BF029215	A1675178	U28386	N42752	K02581	AI525822	AF017790	AA719022	D80008	A1990405	AF098158	AW003586	U73379	A1990026
154 156	157	158	162	153	164	4 7	163	165	159	160	166	167	180	178	177	181	173	176
198 199	200	202	204	205	206	207	208	209	210	211	212	213	214	215	216	217	218	219

Table 1 (Continued)

breast carcinoma amplified sequence 4	breast carcinoma amplified sequence 1	sal-like 4 (Drosophila)	serine/threonine kinase 6	transmembrane prostate androgen induced	KINA	eukaryotic translation elongation factor 1 alpha	2	ESTs	collagen type I alpha 1	KDEL (Lys-Asp-Glu-Leu) endoplasmic	reticulum protein retention receptor 3	· hypothetical protein MGC861	hypothetical protein FLJ20354	unknown	24-dehydrocholesterol reductase	kinesin-like 6 (mitotic centromere-associated	kinesin)	CDC20 cell division cycle 20 homolog (S.	cerevisiae)	ribosomal protein L4	unknown	ESTs	immunoglobulin superfamily member 9	kinase interacting with leukemia-associated	gene (stathmin)	cell division cycle associated 1	similar to rat nuclear ubiquitous casein kinase	2	HSPC150 protein similar to ubiquitin-	centromere protein F 350/400ka (mitosin)	
Hs.56237	Hs.129057	Hs.189095	Hs.250822	Hs.83883		Hs.2642		Hs.224895	Hs.172928	Hs.250696		Hs.208912	Hs.133260	NOLL	Hs.75616	Hs.69360		Hs.82906		Hs.286	NOLL	Hs.133294	Hs.38002	Hs.127310	1	Hs.234545	Hs.118064		Hs.5199	Hs.77204	
q13.13	q13.2	q13.2	q13.31	q13.32		q13.33	٠	q13.33	q13.1	q13.1	•	q13.2	p31.2	p31.3	p32.3	p34.1	•	p34.2		p35.3	q21.3	d22	q23.1	q23.2		q23.3	q32.1		q32.1	q32.3	,
20	20	20	20	20		20		2	22	22		22	<del></del>	<b>~</b> -	<del></del>	~		<del>-</del>		₹-	<del></del>	<del>-</del>	<del>-</del>	~		~	<del>-</del>		<b>~</b>	~	
metastatic	metastatic	metastatic	metastatic	metastatic		metastatic		metastatic	metastatic	metastatic		metastatic	primary	primary	primary	primary	•	primary		primary	primary	primary	primary	primary		primary	primary		primary	primary	•
breast	breast	breast	breast	breast		breast		breast	breast	breast		breast	colon	colon	colon	colon		colon		colon	colon	colon	colon	colon		colon	colon		colon	colon	
AA207074	AF041260	AI638036	AF011468	AA535819		X70940		A1872267	Y15915	AL035081		A1961206	AK000490	R33352	AI739473	U63743		<b>U05340</b>		A1990026	T16144	AW271106	AB037776	AA830844		AA383718	AI380204		AI990409	U30872	
182	174	183	175	172		179		184	186	187		185	241	235	233	239		243		242	234	232	230	236		231	237		240	238	
220	221	222	223	224		225		226	227	228		229	230	231	232	233		234		235	236	237	238	239		240	241		242	243	

Table 1 (Continued)

centromere protein A 17kDa	ribonucieotide reduciase iviz polypepilue	hypothetical protein FLJ25211	TTK protein kinase	ESTs	KIAA0906 protein	collagen type VIII alpha 1	Homo sapiens mRNA full length insert cDNA	clone EUROIMAGE 1913076	epithelial cell transforming sequence 2	oncogene	ESTs	FYN binding protein (FYB-120/130)	cyclin B1	paired-like homeodomain transcription factor 1	RAB6 interacting kinesin-like (rabkinesin6)	kinesin-like 2	Homo sapiens cDNA FLJ11041 fis clone	PLACE1004405	inhibin beta A (activin A activin AB alpha	polypeptide)	anillin actin binding protein (scraps homolog	Drosophila)	anterior gradient 2 homolog (Xenepus laevis)	enhancer of zeste homolog 2 (Drosophila)	Homo sapiens clone IMAGE:5455669 mRNA	partial cds	solute carrier family 39 (zinc transporter)	T.I AK cell-originated protein kinase	pituitary tumor-transforming 1	Sulfatase FP	ים במנספים ה
Hs.1594	Hs./5319	Hs.44269	Hs.169840	Hs.196042	Hs.56966	Hs.114599	Hs.41271		Hs.122579		Hs.195225	Hs.58435	Hs.23960	Hs.84136	Hs.73625	Hs.20830	Hs.28792		Hs.727		Hs.62180		Hs.91011	Hs.77256	Hs.67776		Hs.352415	10. 10.774	Hs 252587	He 70823	15:100
p23.3	p25.1	q33.1	p21.31	p24.3	p25.1	q12.3	q12.3		q26.32		d28	p13.1	q13.2	q31.1	q31.2	p21.32	p14.1	•	p14.1		p14.2		p21.1	q36.1	NOLL		NULL	1,04.4	η23.2 η33.2		<u>.</u>
2	7	7	က	က	က	က	က		က		က	ß	5	2	2	9	7		7		7		7	7	ω		ω	o	ο α	α	<b>ɔ</b> .
primary	primary	primary	primary	primary	primary	primary	primary	•	primary	•	primary	primary	primary	primary	primary	primary	primary	-	primary	•	primary	•	primary	primary	primary	,	primary		primary	primary	
colon	colon	colon	colon	colon	colon	colon	colon		colon		colon	colon	colon	colon	colon	colon	colon		colon		colon		colon	colon	colon		colon	1	בסוסט בסוסט		
U14518	BE966236	AL045632	M86699	A1962335	AB020713	X57527	AI557210		AI823992		AI087975	AW001872	M25753	U70370	AI739117	D14678	AA059458		M13436	-	AI341261		AI922323	U61145	AI949095		AA625199		A1932328	AMZ034/0	AVV045713
284	285	283	302	301	300	304	305	) }	303	) )	299	307	306	308	309	310	3,5	<u>)</u>	315		314		312	311	316		318	ļ	325	524 500	323
244	245	246	247	248	249	250	251		252		253	254	255	256	257	258	259	3	260		261		262	263	264	· 	265		266 267	707	202

Table 1 (Continued)

cyclin E2	mal T-cell differentiation protein 2	squalene epoxidase	hypothetical protein MGC5254	Homo sapiens cDNA FLJ14388 tis clone	HEMBA1002/16	zinc finger DHHC domain containing 12	EST	hypothetical protein FLJ36779	ZW10 interactor	cell division cycle 2 G1 to S and G2 to M	hypothetical protein FLJ10540	KIAA0750 gene product	similar to RIKEN cDNA 2610036L13	serologically defined colon cancer antigen 28	Thy-1 cell surface antigen	H2A histone family member X	forkhead box M1	Rac GTPase activating protein 1	cullin 4A	cyclin-dependent kinase inhibitor 3 (CDK2-	associated dual specificity phosphatase)	cyclin B2	KIAA0101 gene product	protein regulator of cytokinesis 1	HSPC037 protein	tubulin beta 4	Homo sapiens similar to possible G-protein	receptor clone MGC:21993 IMAGE:4398317	mRNA complete cds	hypothetical protein MGC2601	hypothetical protein FLJ30002
Hs.30464	Hs.76550	Hs.71465	Hs.222088	Hs.9812		Hs.133122	Hs.274152	Hs.212613	Hs.42650	Hs.334562	Hs.14559	Hs.314434	Hs.23044	Hs.84700	Hs.125359	Hs.147097	Hs.239	Hs.23900	Hs.183874	Hs.84113		Hs.194698	Hs.81892	Hs.344037	Hs.108196	Hs.159154	Hs.290943			Hs.124915	Hs.351474
q22.1	q24.12	q24.13	q24.13	q24.22		q34.11	q34.3	q34.3	q21.1	q21.2	q23.33	p15.3	q13.1	q13.4	q23.3	q23.3	p13.33	q13.12	q33.3	q22.1		q21.3	q22.2	q25.3	NOLL	NULL	p13.3	•		p13.3	p13.3
∞	∞	∞	∞	∞		တ	0	6	10	10	10	7	7	7	7	7	12	12	13	4		15	15	15	16	16	16			16	16
primary	primary	primary	primary	primary		primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	•	primary	primary	primary	primary	primary	primary	•		primary	primary
colon	colon	colon	colon	colon		colon	colon	colon	colon	colon	colon	colon	colon	colon	colon	colon	colon	colon	colon	colon		colon	colon	colon	colon	colon	colon			colon	colon
AF091433	AL117612	D78130	AI656807	AA147884		AW007586	AI811865	W25552	AF067656	AL524035	AI674163	AB018293	AL079372	D60944	AA704137	X14850	U74612	U82984	AI291142	1.25876		AL080146	D14657	AA195614	BC003186	AW003626	AI701742			BE965311	AL520675
319	321	317	320	322		326	327	328	244	245	246	248	251	247	249	250	253	252	254	255		258	257	256	265	266	259			260	261
269	270	271	272	273		274	275	276	277	278	279	280	281	282	283	284	285	286	287	288	) }	289	290	291	292	293	294			295	296

Table 1 (Continued)

hypothetical protein MGC2605	selenoprotein X 1	hypothetical protein MGC4692	ESTs	solute carrier family 16 (monocarboxylic acid	transporters) member 3	KIAA1618 protein	hypothetical protein BC014072	unknown	topoisomerase (DNA) II alpha 170kDa	ESTs Moderately similar to 1P2A_HUMAN	DNA topoisomerase II alpha isozyme	[H.sapiens]	Homo sapiens Similar to epsin 3 clone	MGC. 1000 IMAGE. 3300439 III. N. A. COMPINED	Homo sapiens cDNA FLJ36569 fis clone	TRACH2010824 highly similar to	Ribonucleoprotein	ESTs Weakly similar to hypothetical protein	FLJ20489 [Homo sapiens] [H.sapiens]	hypothetical protein MGC11138	karyopherin alpha 2 (RAG cohort 1 importin	alpha 1)	hematological and neurological expressed 1	thymidine kinase 1 soluble	highly expressed in cancer rich in leucine	heptad repeats	ubiquitin UBF-fl	KIAA0186 gene product	retinoic acid induced 3	chromosome 20 open reading frame 1
Hs.124015	Hs.279623	Hs.13561	Hs.368078	Hs.85838		Hs.314169	Hs.348504	NOLL	Hs.156346	Hs.370428			Hs.307036		Hs.103512			Hs.165909		Hs.90207	Hs.159557		Hs.109706	Hs.105097	Hs.58169		Hs.288549	Hs.36232	Hs.194691	Hs.9329
p13.3	p13.3	p13.3	q12.2	NULL		NULL	q11.2	q21.31	q21.31	q21.31			q22		q23.2	<u>.</u>		q23.2		q24.2	q24.3	,	q25.3	q25.3	p11.32	•	q13.43	p11.21	p11.23	q11.1
16	16	16	16	17		17.	17	17	17	17			17		17	•		17		17	17		17	17	18		. 19	20	20	20
primary	primary	primary	primary	primary	•	primary	primary	primary	primary	primary			primary		primary			primary		primary	primary	•	primary	primary	primary		primary	primary	primary	primary
colon	Colon	colon	colon	colon		uoloo	colon	colon	colos	colon			colon		colon	3		colon		colon	colon		colon	colon	colon	) )	colon	colon	colon	colon
A1953838	W92110	AI819340	AA904482	U81800		A1683036	RE328850	1 47276	AI375913	AW/003286			BC001038		RE029215	01.0505.10		BG165011		A1675178	U28386		AI525822	K02581	AF017790		AA719022	D80008	A1990405	AF098158
262	263	267	264	276	i	278	275	272	274	280	2		271		260	603		279	ì	777	270		268	273	28.7		282	288	290	291
297	200	2007	300	301		303	305 303	200	30.4 70.5	308	3		307		a C	2		309		310	311		312	313	314	<u>.</u>	315	316	317	318

Table 1 (Continued)

SCAN domain containing 1	ubiquitin-conjugating enzyme E2C	breast carcinoma amplified sequence 4	breast carcinoma amplified sequence 1	serine/threonine kinase 6	transmembrane prostate androgen induced	RNA	eukaryotic translation elongation factor 1 alpha	2	KDEL (Lys-Asp-Glu-Leu) endoplasmic	reticulum protein retention receptor 3	collagen type I alpha 1	hypothetical protein MGC861	hypothetical protein FLJ20354	unknown	24-dehydrocholesterol reductase	kinesin-like 6 (mitotic centromere-associated	kinesin) ,	CDC20 cell division cycle 20 homolog (S.	cerevisiae)	ribosomal protein L4	unknown	ESTs	immunoglobulin superfamily member 9	kinase interacting with leukemia-associated	gene (stathmin)	cell division cycle associated 1	ESTs	cell division cycle associated 1	similar to rat nuclear ubiquitous casein kinase	2	HSPC150 protein similar to ubiquitin-
Hs.274411	Hs.93002	Hs.56237	Hs.129057	Hs.250822	Hs.83883		Hs.2642		Hs.250696		Hs.172928	Hs.208912	Hs.133260	NOLL	Hs.75616	Hs.69360		Hs.82906	,	Hs.286	NULL	Hs.133294	Hs.38002	Hs.127310		Hs.234545	Hs.191187	Hs.234545	Hs.118064		Hs.5199
q11.22	q13.12	q13.13	q13.2	q13.31	q13.32		q13.33		q13.1	•	q13.1	q13.2	p31.2	p31.3	p32.3	p34.1	•	p34.2	•	p35.3	q21.3	d22	q23.1	q23.2		q23.3	q23.3	q23.3	q32.1	•	q32.1
20	20	20	20	20	20		20		22		22	22	_	τ-	_	<del>-</del>		_		~	_	~	_	_		<del></del>	<del>-</del>	~	~		~
primary	primary	primary	primary	primary	primary	•	primary		primary	•	primary	primary	metastatic	metastatic	metastatic	metastatic		metastatic		metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic		metastatic
colon	colon	colon	colon	colon	colon		colon	•	colon		colon	colon	colon	colon	colon	colon		colon		colon	colon	colon	colon	colon		colon	colon	colon	colon		colon
AW003586	U73379	AA207074	AF041260	AF011468	AA535819		X70940		AL035081		Y15916	AI381686	AK000490	R33352	AI739473	U63743	) )	U05340		A1990026	T16144	AW271106	AB037776	AA830844		AF326731	AI983896	AF326731	AI380204		A1990409
287	294	286	293	262	295	) )	289		296	ì	297	298	420	354	351	396		425	ļ	421	352	346	340	357	!	330	341	380	360	) ) }	403
319	320	321	322	323	324	!	325		326	}	327	328	320	330	331	332	!	333	) 1	334	335	336	337	338	}	339	340	341	342	]	343

conjugating enzyme	centromere protein F 350/400ka (mitosin)	centromere protein A 17kDa	ribonucleotide reductase M2 polypeptide	hypothetical protein FLJ25211	TTK protein kinase	ESTs	KIAA0906 protein	collagen type VIII alpha 1	Homo sapiens mRNA full length insert cDNA	clone EUROIMAGE 1913076	ESTs Moderately similar to zinc finger protein	91 (HPF7 HTF10) [Homo sapiens] [H.sapiens]	epithelial cell transforming sequence 2	oncogene	ESTS	FYN binding protein (FYB-120/130)	cyclin B1	paired-like homeodomain transcription factor 1	RAB6 interacting kinesin-like (rabkinesin6)	kinesin-like 2	Homo sapiens cDNA FLJ11041 fis clone	PLACE1004405	Homo sapiens cDNA FLJ11041 fis clone PLACE1004405	inhibin beta A (activin A activin AB alpha	polypopulacy	anilin acun binding protein (scraps nornolog Drosophila)	anillin actin binding protein (scraps homolog Drosophila)	anillin actin binding protein (scraps homolog
	Hs.77204	Hs.1594	Hs.75319	Hs.44269	Hs.169840	Hs.196042	Hs.56966	Hs.114599	Hs.41271		Hs.36830		Hs.122579		Hs.195225	Hs.58435	Hs.23960	Hs.84136	Hs.73625	Hs.20830	Hs.28792		Hs.28792	Hs.727	00.00	HS.62180	Hs.62180	Hs.62180
	q32.3	p23.3	p25.1	q33.1	p21.31	p24.3	p25.1	q12.3	q12.3		q26.1		q26.32		d28	p13.1	q13.2	q31.1	q31.2	p21.32	p14.1		p14.1	p14.1		p14.2	p14.2	p14.2
	~	7	7	7	က	က	က	က	က		က		က		က	2	S	2	2	ၑ	7		7	<b>~</b>	f	_	_	7
	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic		metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	•	metastatic	metastatic	metastatic
	colon	colon	colon	colon	colon	colon	coloo	colon	colon		colon		colon		colon	colon	colon	colon	colon	colon	colon		colon	colon	•	colon	colon	colon
	U30872	U14518	BE966236	AL045632	M86699	A1962335	AB020713	X57527	AI557210		W02608	•	AI823992		AI087975	AW001872	M25753	U70370	AI739117	D14678	AA059458		AI343467	M13436		AK023208	AK023208	AK023208
	382	400	419	349	365	334	333	412	417		344		395		332	409	408	410	434	389	427		436	437		329	438	440
	344	345	346	347	348	349	350	351	352		353		354		355	356	357	358	359	360	361		362	363		364	365	366

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Drosophila) sorting nexin 10	anterior gradient 2 homolog (Xenepus laevis)	collagen type I alpha 2	enhancer of zeste homolog 2 (Drosophila)	Homo sapiens clone IMAGE:5455669 mRNA	partial cds	solute carrier family 39 (zinc transporter)	member 4	T-LAK cell-originated protein kinase	pituitary tumor-transforming 1	sulfatase FP	tumor protein D52	cyclin E2	ESTs	mal T-cell differentiation protein 2	squalene epoxidase	hypothetical protein MGC5254	Homo sapiens cDNA FLJ14388 fis clone	HEMBA1002716	zinc finger DHHC domain containing 12	EST	hypothetical protein FLJ36779	ZW10 interactor	cell division cycle 2 G1 to S and G2 to M	hypothetical protein FLJ10540	Homo sapiens cDNA FLJ32525 fis clone SMINT2000060	KIAA0750 gene product	similar to RIKEN cDNA 2610036L13	serologically defined colon cancer antigen 28	Thy-1 cell surface antigen
L Hs.106260 s		_	Ī	Hs.67776 F	0.	Hs.352415 s	_	Hs.104741 T	Hs.252587 p		Hs.2384 t	_				Hs.222088 h	Hs.9812 I	-	•	Hs.274152 E	~	Hs.42650		Hs.14559	Hs.185918 B	Hs.314434	Hs.23044		Hs.125359 ⁻
015.2	p21.1	q21.3	q36.1	NULL	-	NULL		p21.1	q13.2	q13.3	q21.13	q22.1	q24.11	q24.12	q24.13	q24.13	q24.22	-	q34.11	934.3	q34.3	q21.1	q21.2	q23.33	p15.1	p15.3	q13.1	q13.4	q23.3
7	. ~	_	7	œ		∞.		œ	∞	ω	œ	∞	ω	∞	æ	ω	œ		ග	တ	ග	9	5	9	<del>-</del>	7	7	7	7
metastatic	metastatic	metastatic	metastatic	metastatic		metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic
5		colon	colon	colon		colon		colon	colon	colon	colon	colon	colon	colon	colon	colon	colon		colon	colon	colon	colon	colon	colon	colon	colon	colon	colon	colon
A1085534	AI922323	Al961907	1161145	A1949095		AA625199		A1932328	AA203476	AW043713	AA524023	AF091433	AA610522	AL117612	D78130	A1656807	AA147884		AW007586	AI811865	W25552	AF067656	X05360	AI674163	AA705015	AB018293	AL079372	D60944	AA704137
070	39.5	339	356	336		362	3	439	428	414							80 80	3	374	383	393	355	368	416	337	372	401	350	379
790	368 368	369	370	371	5	372	2	373	374	375	376	377	378	379	380	381	383	200	383	384	385	386	387	388	389	390	391	392	393

H2A histone family member X forkhead box M1 Rac GTPase activating protein 1 Human clone 295 5cM region surrounding hepatocyte nuclear factor-1a/MODY3 mRNA	cullin 4A cyclin-dependent kinase inhibitor 3 (CDK2- associated dual specificity phosphatase)	cyciiii bz KIAA0101 gene product protein regulator of cytokinesis 1 HSPC037 protein	tubulin beta 4: Homo sapiens similar to possible G-protein receptor clone MGC:21993 IMAGE:4398317 mRNA complete cds	hypothetical protein MGC2601 hypothetical protein FLJ30002 hypothetical protein MGC2605 selenoprotein X 1 hypothetical protein MGC4692	ESTs solute carrier family 16 (monocarboxylic acid transporters) member 3 KIAA1618 protein hypothetical protein BC014072	topoisomerase (DNA) II alpha 170kDa topoisomerately similar to TP2A_HUMAN DNA topoisomerase II alpha isozyme [H.sapiens] Homo sapiens Similar to epsin 3 clone
Hs.147097 Hs.239 Hs.23900 Hs.204166	Hs.183874 Hs.84113	Hs. 134030 Hs.81892 Hs.344037 Hs.108196	Hs.159154 Hs.290943	Hs. 124915 Hs. 351474 Hs. 124015 Hs. 279623 Hs. 13561	Hs.368078 Hs.85838 Hs.314169 Hs.348504	Hs. 370428 Hs. 370428 Hs. 307036
q23.3 p13.33 q13.12 q24.31	q33.3 q22.1	92.2 922.2 925.3 NULL	NULL p13.3	0 13.3 0 13.3 0 13.3 0 13.3 0 13.3 0 13.3	A12.2 NULL A11.2	q21.31 q21.31 q22
<del>2</del> 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	<u>6</u> 4 4	<u> </u>	10 10	9 9 9 9 9	14 7 14	1 1 1 1 2 2
metastatic metastatic metastatic metastatic	metastatic metastatic	metastatic metastatic metastatic metastatic	metastatic metastatic	metastatic metastatic metastatic metastatic metastatic	metastatic metastatic metastatic	metastatic metastatic metastatic
colon colon colon	colon		colon	colon colon colon	colon colon colon	colon
X14850 U74612 U82984 R61322	AI291142 L25876	ALUSO 146 D14657 AA195614 BC003186	AW003626 AI701742	BE965311 AL520675 Al953838 W92110 Al819340	AA904482 U81800 AI683036 BE328850	Al375913 AW003286 BC001038
381 429 384 343	353	413 406 407	415 358	364 364 377 385 431	405 391 411 390	375 375
394 395 396 397	398	4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	404 405	406 407 408 410	14 4 4 4 12 12 14 4 4	514 714 814 814

Table 1 (Continued)

MGC:1006 IMAGE:3505495 mRNA complete cds Homo sapiens cDNA FLJ36569 fis clone TRACH2010824 highly similar to	ESTs Weakly similar to hypothetical protein FLJ20489 [Homo sapiens] [H.sapiens]	hypothetical protein MGC11138 karyopherin alpha 2 (RAG cohort 1 importin alpha 1)	hematological and neurological expressed thymidine kinase 1 soluble highly expressed in cancer rich in leucine heptad repeats	highly expressed in cancer rich in leucine heptad repeats	ubiquitin UBF-fl KIAA0186 gene product retinoic acid induced 3 chromosome 20 open reading frame 1 SCAN domain containing 1 ubiquitin-conjugating enzyme E2C breast carcinoma amplified sequence 4 breast carcinoma amplified sequence 1 serine/threonine kinase 6 transmembrane prostate androgen induced RNA eukaryotic translation elongation factor 1 alpha 2 KDEL (Lys-Asp-Glu-Leu) endoplasmic reticulum protein retention receptor 3 collagen type 1 alpha 1	
Hs.103512	Hs.165909	Hs.90207 Hs.159557	Hs.109706 Hs.105097 Hs.58169	Hs.58169	Hs.288549 Hs.36232 Hs.194691 Hs.194691 Hs.274411 Hs.274411 Hs.26237 Hs.250822 Hs.83883 Hs.250696 Hs.250696	2 2
q23.2	q23.2	q24.2 q24.3	q25.3 q25.3 p11.32	p11.32	913.43 911.23 911.12 913.12 913.13 913.33 913.33	- - - -
17	17	17	17 17 18	18	19 20 20 20 20 20 20 20 20 20 20 20 20 20	77
metastatic	metastatic	metastatic metastatic	metastatic metastatic metastatic	metastatic	metastatic metastatic metastatic metastatic metastatic metastatic metastatic metastatic metastatic metastatic	metastatic
colon	colon	colon	colon colon colon	colon	colon colon colon colon colon colon colon colon colon colon	colon
BF029215	BG165011	AI675178 U28386	AI525822 K02581 AF017790	AF017790	AA719022 D80008 AI990405 AF098158 AW003586 U73379 AA207074 AF041260 AF011468 AA535819 X70940	Y15916
359	426	398 369	335 378 331	404	422 371 399 402 370 433 438 430 424 435 394	397
419	420	421 422	423 424 425	426	427 428 429 431 432 433 435 435 435 435	439

Table 1 (Continued)

hypothetical protein MGC861	ESTs	ESTs	ESTs	Homo sapiens cDNA FLJ13017 fis clone NT2RP3000628	Homo sapiens cDNA FLJ13536 fis clone DI ACE1006521	PDZ domain protein (Drosophila inaD-like)	beta-amyloid binding protein precursor	ESTs	Homo sapiens cDNA FLJ12095 fis clone	nEivide (002010 n53.regulated DDA3	ביים ביים ביים ביים ביים ביים ביים ביים	ESIS	apolipoprotein A-I binding protein	hypothetical protein MGC13038	cell division cycle associated 1	uridine monophosphate kinase	chromosome 1 open reading frame 19	unknown	methylene tetrahydrofolate dehydrogenase	(NAD+ dependent) methenyltetrahydrofolate	cyclohydrolase	Homo sapiens Similar to RIKEN cDNA	2510006C20 gene clone MGC:24001	IMAGE:4050858 mRNA complete cds	ribonucleotide reductase M2 polypeptide	unknown	cell division cycle associated 7	ESTs Weakly similar to hypothetical protein	FLJ20837 [Homo sapiens] [H.sapiens]
Hs.208912	Hs.145958	Hs.120893	Hs.259438	Hs.301858	Hs.11493	Hs.321197	Hs.333541	Hs.127274	Hs.301237	Uc 77550	13.7.5	Hs.133294	Hs.374850	Hs.158515	Hs.234545	Hs.75939	Hs.32058	NOLL	Hs.154672			Hs.105223			Hs.75319	NULL	Hs.333893	Hs.144264	
q13.2	p31.3	p31.3	p31.3	p31.3	p31.3	p31.3	p32.1	p32.1	p32.1	204.2	0.1.3 0.1.3	q22	q22	<b>4</b> 22	q23.3	q23.3	q25.3	p11.1	p13.1			p16.2	•		p25.1	q13	q31.1	p13.2	
22	_	<del>-</del>	~	<del></del>	~	_	_	_	~	*	_	<del>-</del>	<del>-</del>	τ	<del>-</del>	<del>-</del>	<del>-</del>	7	7			8			7	7	7	2	
metastatic	primary	primary	primary	primary	primary	primary	primary	primary	primary	1	לומווק	primary	primary	primary	primary	primary	primary	primary	primary			primary	•		primary	primary	primary	primary	
colon	lung	lung	lung	lung	lung	lung	lung	lung	lung	!	Buni	lung	lung	lung	lung	junj	lung	lung	lung	,		lung			lung	lung	lung	lung	
AI381686	AA905821	A1056599	AW070459	AK022113	AU151151	AB044807	AA012917	BF224444	AU147177		AA9Z0909	AI053741	AI766666	AI739071	AF326731	BC002906	AA182412	AA725362	A1990317			AI191897			AI492879	H24953	AA749314	C00851	
418	506	508	511	527	528	547	485	498	526	į	4/3 د	443	448	469	441	446	442	482	472			464			474	481	451	519	
440	441	442	443	444	445	446	447	448	449	Ç.	450	451	452	453	454	455	456	457	458			459	}		460	461	462	463	

ESTs	peptidylprolyl isomerase (cyclophilin)-like 1	high mobility group AT-hook 1		SRY (sex determining region Y)-box 4	hypothetical protein FLJ20958	hypothetical protein LOC51256	hypothetical protein MGC1223	epidermal growth factor receptor	(erythroblastic leukemia viral (v-erb-b)	oncogene homolog avian)	ESTs	ESTs	ESTs	ESTs	Homo sapiens clone MGC:33530	IMAGE:4820705 mRNA complete cds	LanC lantibiotic synthetase component C-like	2 (bacterial)	Homo sapiens cDNA FLJ10417 fis clone	N   2KP 1000112	biliverdin reductase A	ESTs	ESTs	ESTs	ESTs Moderately similar to cytokine receptor-	like factor 2 cytokine receptor CRL2 precusor	[Homo sapiens]	histone H2A.F/Z variant	Homo sapiens cDNA: FLJ21623 fis clone	Homo sapiens mRNA cDNA DKFZp434A1014
Hs.125249	Hs.27693	Hs.139800	Hs.201619	Hs.83484	Hs.261023	Hs.8645	Hs.273077	Hs.77432		•	Hs.127991	Hs.252928	Hs.205559	Hs.103351	Hs.335933		Hs.134342	•	Hs.180171		Hs.81029	Hs.284148	Hs.296098	Hs.152895	Hs.222015			Hs.301005	Hs.306791	Hs.332520
p15.1	p21.2	p21.31	p22.3	p22.3	p23	p24.1	p24.2	p11.2			p11.2	p11.2	p11.2	p11.2	p11.2		p11.2		p12.3		p13	p13	p13	p13	p13			p13	p13	p13
2	ဖ	9	ဖ	9	9	ၑ	9	_			7	7	7	7	7		7		7		7	7	7	7	7			7	7	7
primary	primary	primary	primary	primary	primary	primary	primary	primary			primary	primary	primary	primary	primary		primary		primary		primary	primary	primary	primary	primary			primary	primary	primary
lung	lung	lung	lung	lung	lung	lung	lung	lung	•		lung	lung	lung	lung	lung		lung		lung		lung	lung	lung	lung	lung			lung	lung	lung
AA383208	AA524353	AW005489	AI677701	BG528420	AI439141	AI279547	W27692	K03193			A1806160	AW138673	H65306	AW971863	D60436		AI363001		AV700815		AA740186	AI252004	AW452419	AI418313	AI191118			AI823792	AK025276	AL137266
458	548	522	538	551	467	539	540	495			496	497	502	509	536		545		524		486	510	514	515	517			523	533	534
464	465	466	467	468	469	470	471	472			473	474	475	476	477		478		479		480	481	482	483	484			485	486	487

Table 1 (Continued)

(from clone DKFZp434A1014) partial cds	hypothetical protein MGC4607	NPC1 (Niemann-Pick disease type C1 gene)- like 1	serine/threonine kinase 17a (apoptosis-	inaucing)	hypothetical protein MGC2821	IGF-II mRNA-binding protein 3	hypothetical protein BC012331	membrane protein palmitoylated 6 (MAGUK	p55 subfamily member 6)	DNA directed RNA polymerase II polypeptide	J-related gene	scribble	carbonic anhydrase VIII	ESTs	ESTs	pituitary tumor-transforming 1	unknown	unknown	Homo sapiens mRNA cDNA DKFZp566A1046	(from clone DKFZp566A1046)	ESTs	ESTs	Homo sapiens cDNA FLJ14180 fis clone NT2RD2003799		Homo sapiens cDNA FLJ34367 fis clone FEBRA2016621	tumor protein D52	ESTs	cadherin 17 Ll cadherin (liver-intestine)	cyclin E2
	Hs.9960	Hs.47701	Hs.9075		Hs.59594	Hs.79440	Hs.87385	Hs.108931		Hs.375569		Hs.239784	Hs.250502	Hs.12664	Hs.19107	Hs.252587	NOLL	NOLL	Hs.168950		Hs.133293	Hs.128841	Hs.296753	70000	Hs.60681	Hs.2384	Hs.184387	Hs.89436	Hs.30464
	p13	p13	p13	•	p14.1	p15.3	p15.3	p15.3		q22.1		NULL	q12.2	q13.2	q13.2	q13.2	q13.3	q13.3	q21.11		q21.11	q21.11	q21.11	;	q21.11	q21.13	q21.13	q22.1	q22.1
	7	^	7	ı	/	/	/	7		7		ω	ω	ω	ω	ω	ω	∞	∞		∞	∞	ω	•	$\infty$	∞	ω	ω	ω
	primary	primary	primary	•	primary	primary	primary	primary		primary		primary	primary	primary	primary	primary	primary	primary	primary		primary	primary	primary	•	primary	primary	primary	primary	primary
	lung	lung	lung		lung	lung	lung	lung		lung		lung	fung	lung	lung	lung	lung	lung	lung		lung	lung	gunj	-	lung	lung	lung	lung	lung
	BC004903	AF192523	AW194730		BC000769	U97188	AI910524	AI806483		AW402635		AI922792	R51273	BE465243	AA132172	AA203476	AF232217	AF130055	BF002104		AI335223	AI370381	AK024242		AI/01468	BG389015	AA479492	007969	AF091433
	545	546	220		541	445	465	471		494		475	489	200	503	549	555	556	463		202	512	529	Č	230	480	499	488	491
	488	489	490	•	491	492	493	494		495		496	497	498	499	200	501	502	503		504	505	206	1	207	208	209	510	511

Table 1 (Continued)

collagen triple helix repeat containing 1	ESTs	hypothetical protein MGC5254	development and differentiation enhancing	factor 1	ESTs Weakly similar to hypothetical protein	FLJ20489 [Homo sapiens] [n.sapiens]	KIAA1485 protein	Homo sapiens mRNA cDNA DKFZp451M139	(from clone DKFZp451M139)	hypothetical protein FLJ11088	DKFZP564O1863 protein	hypothetical protein FLJ10637	KIAA1340 protein	serine/threonine kinase 38 like	SRB7 suppressor of RNA polymerase B	homolog (yeast)	unknown	ESTs	Homo sapiens cDNA FLJ11335 fis clone	PLACE1010630	Homo sapiens cDNA FLJ34764 fis clone NT2NE2002311	transcription factor BMAL2	branched chain aminotransferase 1 cytosolic	Homo sapiens cDNA FLJ13318 fis clone OVARC1001600	Homo sapiens cDNA: FLJ21962 fis clone HEP05564	Homo sapiens mRNA cDNA DKFZp564F2072	(from clone DKFZp564F2072)	hypothetical protein MGC10946
Hs.283713	Hs.130107	Hs.222088	Hs.10669		Hs.20247		Hs.15611	Hs.176669		Hs.227591	Hs.173074	Hs.22595	Hs.51743	Hs.184523	Hs.286145		NOLL	Hs.221024	Hs.284270		Hs.111583	Hs.222024	Hs.317432	Hs.296734	Hs.7567	Hs.301210		Hs.170994
q22.3	q22.3	q24.13	q24.22		q24.22		q24.22	q24.23	-	p11.22	p11.23	p11.23	p11.23	p11.23	p11.23	•	p11.23	p11.23	p11.23		p11.23	p11.23	p12.1	p12.1	p12.1	p12.1	•	p12.1
ω	∞	∞	∞		œ		∞	∞		12	12	12	12	12	12		12	12	1	!	12	12	12	12	12	12		12
primary	primary	primary	primary		primary		primary	primary		primary	primary	primary	primary	primary	primary		primary	primary	primary		primary	nrimary	primary	primary	primary	primary		primary
luna	n bun	luna	lung		lung		lund		9	lund	Pind	bun	Ing	lund	ling	2	lund	lund	בי בי	2	lung	ם ו		lung	lung	וווים	D 5	lung
AA584310	AA904882	AA451665	W03103		BF055351		BF941325	AW/137073		AA447947	R91766	AF274950	A1334297	AW779556	A1688580		AF161472	RF724206	AI 118653	AL 19003	AI652982	A 4127950	A1652662	AU154905	AK025615	AA829940		BE326710
490	505	543	493		518		544	53.5	3	537	456	466	470	476	478	ř	483	70 Z	700	020	531	7,7	225	460	461	462	1	468
510	2 7. 7 4.	7 7	515	· ·	516		517	χ 2 2	2	710	500	521	522	525 533	524	170	525	526	250	170	528	200	520	531	532	533	3	534

Table 1 (Continued)

v-Ki-ras2 Kirsten rat sarcoma 2 viral oncogene	ESTS	ESTs	ethanolamine kinase	ubiquitin-like containing PHD and RING finger	domains 1	H2A histone family member J	C2f protein	DEAD/H (Asp-Glu-Ala-Asp/His) box	polypeptide 11 (CHL1-like helicase homolog S.	cerevisiae)	forkhead box M1	cyclin-dependent kinase inhibitor 3 (CDK2-	associated dual specificity phosphatase)	androgen-regulated short-chain	dehydrogenase/reductase 1	ESTs	Homo sapiens cDNA FLJ36057 fis clone	TESTI2018475 highly similar to LAMININ	ALPHA-1 CHAIN PRÉCURSOR	highly expressed in cancer rich in leucine	heptad repeats	BTB (POZ) domain containing 3	ESTS	synaptosomal-associated protein 25kDa	chromogranin B (secretogranin 1)	chromosome 20 open reading frame 139	chromosome 20 open reading frame 97	solute carrier family 4 sodium bicarbonate	transporter-like member 11	transcription factor AP-2 gamma (activating
Hs.351221	Hs.58086	Hs.137003	Hs.120439	Hs.108106		Hs.36727	Hs.12045	Hs.380623			Hs.239	Hs.84113		Hs.179817		Hs.373550	Hs.48659			Hs.58169		Hs.7935	Hs.70903	Hs.84389	Hs.2281	Hs.135056	Hs.26802	Hs.105607	:	Hs.61796
p12.1	p12.1	p12.1	p12.1	p12.2		p12.3	p13.31	p13.31			p13.33	q22.1		q23.2		p11.31	p11.31	•		p11.32		p12.2	p12.2	p12.2	p12.3	p13	p13	p13	•	q13.31
.12	12	12	12	12		12	72	12			12	14		14		78	18			18		20	20	20	20	20	20	20		20
primary	primary	primary	primary	primary		primary	primary	primary	•		primary	primary		primary		primary	primary	•		primary		primary	primary	primary	primary	primary	primary	primary	•	primary
lung	lung	lung	lung	lung		lung	lung	lung			lung	lung		lung		lung	lung	•		lung		lung	lung	lung	lung	lung	lung	lung		lung
AA015609	W70242	AI242023	AI003792	AA669106		BC003602	AI392836	AI983033			<b>U74612</b>	AF213033		AF167438		AI146765	AW003207			AF017790		AB023169	AI732446	D21267	Y00064	AI096882	A1949781	AI924533	( L (	U85658
484	501	516	520	554		459	487	492			521	455		447		513	532			444		450	457	479	452	453	454	477	C L	225
535	536	537	538	539		540	541	545			543	544		545		546	547			548		549	220	551	552	553	554	555	Ç L	556

enhancer binding protein 2 gamma)	heparan sulfate 2-0-sulfotransferase 1	ESTs Moderately similar to hypothetical	protein FLJ20378 [Homo sapiens] [H.sapiens]	hypothetical protein FLJ20354	G-protein gamma-12 subunit	PAI-1 mRNA-binding protein	Homo sapiens cDNA: FLJ23597 fis clone	LNG15281	Fas (TNFRSF6) associated factor 1	DKFZP727A071 protein	unknown	p53-regulated DDA3	apolipoprotein A-I binding protein	ESTs	hypothetical protein MGC13038	cell division cycle associated 1	uridine monophosphate kinase	chromosome 1 open reading frame 19	unknown	methylene tetrahydrofolate dehydrogenase	(NAD+ dependent) methenyltetrahydrofolate	cyclohydrolase	Homo sapiens Similar to RIKEN cDNA	2510006C20 gene clone MGC:24001	IMAGE:4050858 mRNA complete cds	ribonucleotide reductase M2 polypeptide	unknown	cell division cycle associated 7	ESTs	hypothetical protein FLJ20958
	Hs.169939	Hs.374411		Hs.133260	Hs.8107	Hs.165998	Hs.299254	0	HS.25821	Hs.13036	NOLL	Hs.77550	Hs.374850	Hs.133294	Hs.158515	Hs.234545	Hs.75939	Hs.32058	NOLL	Hs.154672			Hs.105223			Hs.75319	NULL	Hs.333893	Hs.125249	Hs.261023
	p22.3	p31.1		p31.2	p31.2	p31.2	p32.1	6	p32.3	p32.3	p34.1	q21.3	q22	d22	q22	q23.3	q23.3	q25.3	p11.1	p13.1			p16.2			p25.1	q13	q31.1	p15.1	p23
	<del></del>	~		~	_	<del>-</del>	<del></del>	,	_	<del>-</del>	<del>-</del>	τ-	<del></del>	_	_	_	₹-	₹	7	7			7			7	7	7	5	9
	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	:	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic			metastatic			metastatic	metastatic	metastatic	metastatic	metastatic
•	lung	lung		lung	lung	gun	lung	-	lung	lung	lung	lung	lung	lung	lung	lung	lung	lung	lung	lung			gun			gun	lung	lung	lung	lung
	AW151887	BE645144		AI810054	N32508	BC002488	AA618420	0000777410	AW140098	AW409848	AF151063	AA926959	AI766666	AI690773	AI739071	AF326731	D78335	AA182412	AA725362	Al990317			AI191897			BC001886	H24953	AA749314	AA868748	Al439141
	654	651		619	629	636	628	1	179	648	637	009	9/9	588	601	561	262	558	599	592			603		,	583	605	575	579	589
	222	258		228	260	561	562	ç	503	564	565	266	267	268	269	220	571	572	573	574			275		!	9/9	27.7	278	279	280

Table 1 (Continued)

<u>Б</u>		ഉ	<u>a</u>	Φ	ا (zeta			e E	golot			GUK			<b>9</b>		n factor					gene
Homo sapiens cDNA FLJ13503 fis clone PLACE1004838	unknown	Homo sapiens cDNA FLJ25559 fis clone JTH02834	Homo sapiens cDNA FLJ20099 fis clone COL04544	Homo sapiens cDNA FLJ12308 fis clone MAMMA1001931	chaperonin containing TCP1 subunit 6A (zeta 1)	epidermal growth factor receptor	(erythroblastic leukemia viral (v-erb-b) oncogene homolog avian)	Homo sapiens cDNA: FLJ23165 fis clone LNG09846	anillin actin binding protein (scraps homolog Drosophila)	IGF-II mRNA-binding protein 3	hypothetical protein BC012331	membrane protein palmitoylated 6 (MAGUK	p55 subfamily member 6)	claudin 12	Homo sapiens cDNA: FLJ23160 fis clone LNG09682	unknown	met proto-oncogene (hepatocyte growth factor	receptor)	putative methyltransferase	secretory protein SEC8	scribble	cDNA for differentially expressed CO16 gene
Hs.287577	NOLL	Hs.140489	Hs.272227	Hs.188082	Hs.82916	Hs.77432		Hs.279898	Hs.62180	Hs.79440	Hs.87385	Hs.108931		Hs.258576	Hs.118258	NOLL	Hs.285754		Hs.233694	Hs.107394	Hs.239784	Hs.69517
p11.2	p11.2	p11.2	p11.2	p11.2	p11.2	p11.2		p11.2	p14.2	p15.3	p15.3	p15.3		q21.13	q21.13	q31.2	q31.2		q32.1	d33	NULL	NOLL
7	_	7	7	7	/	7		7	7	7	7	7		7	7	7	^		_	7	ω	∞
metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic
lung	lung	lung	lung	lung	lung	lung		lung	lung	lung	lung	lung		lung	lung	gunj	lung		gun!	lung	lung	lung
AU156822	U48722	AA768884	AK000106	AU147861	BE737030	AW157070		BE878463	AK023208	U97188	AI910524	AI806483		AL136770	BF680588	U19348	BG170541		AI632244	A1964022	AI922792	AA723810
909	209	609	610	613	616	622		639	257	260	277	290		617	635	618	638		641	653	593	644
581	582	583	584	585	586	287		288	589	230	591	292	,	593	594	292	296	[	597	598	299	009

ESTs	ESTs	aspartate beta-hydroxylase	ring finger protein 29	Homo sapiens mRNA cDNA DKFZp566A1046	(from clone DKFZp566A1046)	Homo sapiens cDNA: FLJ21569 fis clone	COL06508	hypothetical protein FLJ11011	ESTs Weakly similar to retinal short-chain	dehydrogenase/reductase retSDR2 [Homo	sapiens] [H.sapiens]	transcription elongation factor B (SIII)	polypeptide 1 (15kDa elongin C)	staufen RNA binding protein homolog 2	(Drosophila)	tumor protein D52	hypothetical protein MGC22825	zinc finger protein RINZF	Homo sapiens cDNA FLJ23705 fis clone	HEP11066	calcitonin/calcitonin-related polypeptide alpha	transcription factor BMAL2	hypothetical protein FLJ10637	unknown	SRB7 suppressor of RNA polymerase B	homolog (yeast)	DKFZP564O1863 protein	KIAA1340 protein	serine/threonine kinase 38 like	Homo sapiens cDNA FLJ34764 fis clone	NT2NE2002311
Hs.29419	Hs.152409	Hs.283664	Hs.85524	Hs.168950		Hs.121194		Hs.21275	Hs.356086			Hs.184693		Hs.96870		Hs.2384	Hs.183861	Hs.237146	Hs.49136		Hs.37058	Hs.222024	Hs.22595	NOLL	Hs.286145		Hs.173074	Hs.51743	Hs.184523	Hs.111583	
q12.3	q12.3	q12.3	q13.1	q21.11		q21.11		q21.11	q21.11			q21.11	Ī	q21.11		q21.13	q21.13	q21.13	q24.21		p15.2	p11.23	p11.23	p11.23	p11.23		p11.23	p11.23	p11.23	p11.23	
ω	∞	ω	∞	∞		ω		œ	∞			ω		ω		ω	ω	ω	ω		7	12	12	15	12		7	12	12	12	
metastatic	metastatic	metastatic	metastatic	metastatic		metastatic		metastatic	metastatic			metastatic		metastatic		metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	
lung	lung	lung	lung	lung	ı	lung		lung	lung			lung	•	lung		lung	lung	lung	lung	•	lung	lung	lung	lung	lung		lung	lung	lung	lung	
BF059124	AA543030	AF289489	AW663544	BF002104		AI916600		AI625741	AW150720			N89607		W46994		BG389015	AK000049	AK024296	AL039862		M26095	AF256215	AI569851	AF161472	U46837		R91766	AI334297	AW779556	BF540749	
621	631	632	646	581		612		623	630			645		650		563	633	634	929		611	565	266	573	574		580	584	585	586	
601	602	603	604	605		909		209	809			609		610		611	612	613	614		615	616	617	618	619		620	621	622	623	

Table 1 (Continued)

seven transmembrane protein TM7SF3	Homo sapiens cDNA: FLJ21962 fis clone HEP05564	hypothetical protein MGC10946	Homo sapiens mixiva cuiva unrzpootrzorz (from clone DKFZp564F2072)	v-Ki-ras2 Kirsten rat sarcoma 2 viral oncogene	homolog	Homo sapiens cDNA FLJ13318 fis clone OVARC1001600	ubiquitin-like containing PHD and RING finger	domains 1	H2A histone family member J	Homo sapiens cDNA FLJ36082 fis clone	TESTI2019998	bromodomain adjacent to zinc finger domain	. Y	ESTs	ERO1-like (S. cerevisiae)	hypothetical protein FLJ12618	WW45 protein	cyclin-dependent kinase inhibitor 3 (CDK2-	associated dual specificity phosphatase)	glia maturation factor beta	glutathione peroxidase 2 (gastrointestinal)	ESTs	androgen-regulated short-chain	dehydrogenase/reductase 1	Homo sapiens cDNA FLJ37574 fis clone BRCOC2003100	hypothetical protein FLJ39091
Hs.10071	Hs.7567	Hs.170994	HS.301210	Hs.351221		Hs.296734	Hs.108106		Hs.36727	Hs.322679		Hs.8858		Hs.146134	Hs.25740	Hs.222021	Hs.288906	Hs.84113		Hs.151413	Hs.2704	Hs.97849	Hs.179817		Hs.43397	Hs.98365
p11.23	p12.1	p12.1	p12.1	p12.1		p12.1	p12.2		p12.3	p13.1		q12		q13.1	q21.3	q21.3	q21.3	q22.1		q22.1	q23.1	q23.1	q23.2		q23.2	q24.2
5 5	7 2	24	7	12		7	7		12	12		4		4	4	4	14	4		4	4	4	4		4	4
metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic		metastatic	metastatic		metastatic		metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic		metastatic	metastatic
lung	gun gun	lung	gun Bun	lung	•	lung	lung	•	lung	lung		lung		lung	lung	lung	lung	lung	•	lung	lung	lung	lung	ı	lung	lung
BC005176	AK025615	BE326710	AA829940	AA015609		AU154905	AK025578		BC003602	AI743489		AA102574		A1953589	AW268365	BC006117	AJ292969	AF213033		BC005359	AI985034	AI554514	AF167438		AI654093	BE465894
587	568	570	262	597		604	571		578	643		642		620	809	626	655	267		652	614	624	569		625	647
624	626 626	627	879	629		630	631		632	633		634		635	636	637	638	639		640	641	642	643		644	645

Table 1 (Continued)

chromogranin A (parathyroid secretory protein 1)	hypothetical protein FLJ21916	Homo sapiens cDNA FLJ40513 tis clone TESTI2046456	highly expressed in cancer rich in leucine heptad repeats	synaptosomal-associated protein 25kDa	ESTs	BTB (POZ) domain containing 3	chromogranin B (secretogranin 1)	chromosome 20 open reading frame 97	solute carrier tamily 4 sodium bicarbonate transporter-like member 11	chromosome 20 open reading frame 139	hypothetical protein FLJ20354	ESTs	ESTs	kinase interacting with leukemia-associated	gene (stathmin)	cell division cycle associated 1	HSPC150 protein similar to ubiquitin-	conjugating enzyme	centromere protein F 350/400ka (mitosin)	ribonucleotide reductase M2 polypeptide	hairy and enhancer of split 6 (Drosophila)	cyclin B1	paired-like homeodomain transcription factor 1	hypothetical protein BC003515	Homo sapiens cDNA FLJ11041 tis clone PLACE1004405	inhibin beta A (activin A activin AB alpha
Hs.172216	Hs.90034	Hs.374662	Hs.58169	Hs.84389	Hs.70903	Hs.7935	Hs.2281	Hs.26802	Hs.105607	Hs.135056	Hs.133260	Hs.133294	Hs.133294	Hs.127310		Hs.234545	Hs.5199		Hs.77204	Hs.75319	Hs.42949	Hs.23960	Hs.84136	Hs.284207	Hs.28792	Hs.727
q32.11	q32.11	q32.12	p11.32	p12.2	p12.2	p12.2	p12.3	p13	p13	p13	p31.2	g22	g22	g23.2	-	q23.3	q32.1	•	q32.3	p25.1	q37.3	q13.2	q31.1	p21.2	p14.1	p14.1
4	4	4	18	20	20	20	20	20	20	20	~	~	~	<del>-</del>	•	~	~		_	~	7	2	5	တ	/	7
metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	primary	primary	primary	primary		primary	primary		primary	primary				primary	primary	primary
lung	lung	gunl	lung	Jung	lung	nug	nug	lung	lung	lund	prostate		prostate	prostate	200	prostate	prostate	<u>.</u>	prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate
A1969102	AI656232	AI670847	AF017790	D21267	AI732446	AB023169	Y00064	AI949781	AF336127	A1096882	AKOOO490	AW/271106	A105274.1	A A B 30844	1100000	AF326731	AB032931		U30872	AI492879	N21131	BE407516	U70370	BE794699	AI343467	M13436
615	640	649	559	591	598	602	572	582	594	596	660	650		900	3	657	66.1		658	684	683	690	691	692	694	695
646	647	648	649	650	651	652	653	654	655	656	922 847	2 2 2	000	6 G	900	661	662	1	663	664	665	999	299	999	699	029

Table 1 (Continued)

polypeptide) anillia actin hinding protein (scraps homolog	Drosophila)	T-LAK cell-originated protein kinase	pituitary tumor-transforming 1	hypothetical protein MGC5254	Homo sapiens Similar to RIKEN cDNA	3321402G02 gene clone MGC:23929	IMAGE:4807540 mRNA complete cds	ESTs Weakly similar to T2D3_HUMAN	Franscription initiation factor TFIID 135 kDa	subunit (TAFII-135) (TAFII135)	cell division cycle 2 G1 to S and G2 to M	hypothetical protein FLJ10540	similar to RIKEN cDNA 2610036L13	forkhead box M1	Human clone 295 5cM region surrounding	hepatocyte nuclear factor-1a/MODY3 mRNA	cyclin-dependent kinase inhibitor 3 (CDK2-	associated dual specificity phosphatase)	MAD2 mitotic arrest deficient-like 1 (yeast)	cyclin B2	KIAA0101 gene product	solute carrier family 7 (cationic amino acid	transporter y+ system) member 5	hypothetical protein MGC4692	hypothetical protein BC014072	mitotic spindle coiled-coil related protein	ESTs Moderately similar to TP2A_HUMAN	DNA topoisomerase II alpha isozyme	[H.sapiens]	topoisomerase (DNA) II alpha 170kDa	
Pooly!	Org	7-	pitui	hyp	Hon	332	MA	EST	Trar	qns	Sell Sell	hyp	Simi	fork			ਨੂੰ	ass	MA			solu	tran	hyp					Ë		
U2 62180	13.02 100	Hs.104741	Hs.252587	Hs.222088	Hs 352417			Hs.323445			Hs.334562	Hs.14559	Hs.23044	Hs.239	Hs 204166		Hs.84113		Hs.79078	Hs.194698	Hs.81892	Hs. 184601		Hs.13561	Hs.348504	Hs.16244	Hs 370428			Hs.156346	
7	p 14.2	p21.1	a13.2	n24 13	423.7	1.00		034.3	) : :		q21.2	g23.33	a13.1	p13.33	n24.31	7.5	a22.1		q23.1	g21.3	922.2	I I		p13.3	a11.2	011.2	n21.31	<u>}</u>		q21.31	
ī	,	<b>∞</b>	ω	α	0	9		<b>o</b> :	•		10	10	. <del>L</del>	. 6	5	7	14	_	4	15	15	, <del>c</del>		16	17	17	17	-		17	
	primary	primary	primary	yamina y	primary primary	piniary		nrimary			primary	primary	primary	primary	primary	pillaly	nriman/	) 	primary	primary	primary	primary		primary	primary	primary	primary.	pillialy		primary	
,	prostate	proctate	prostate	prostato	prostate	prostate		nroctata	prostate		prostate	prostate	prostate	prostate	piostate	prostate	orototo.	שומסומים	prostate	prostate	proctate	prostate	אוספומוס	prostate	prostate	prostate	process	piostate		prostate	
	AK023208	V1037378	A1332320	A-KO3410	AI925565	BE544837		1003284	Alsosto		X05360	A1674163	A10/4/103	174647	0/4012	K61322	27030	0/0077	1185410	AL 080146	D44657	A DO14000	Aborroos	A1810340	DE228850	A E G 6 3 3 0 8	2000000	AW003280		AI375913	
	693	000	080	700	969	99			880		667	1 4 9 9	000	000	200	899	Č	600	670	7 7 2	- 62	7/0	4	673	2 0	070	010	9/9		680	
	671	7	7/0	0/3	674	675		7	9/9		677	010	010	6/0	980	681	Ö	789	600	200	400	000	000	202	000	0 0	600 600	069		691	

Table 1 (Continued)

unknown	ESTs Weakly similar to hypothetical protein	FLJ20489 [Homo sapiens] [H.sapiens]	ESTs	ubiquitin UBF-fl	KIAA0186 gene product	chromosome 20 open reading frame 1	ubiquitin-conjugating enzyme E2C	serine/threonine kinase 6	holocarboxylase synthetase (biotin-[proprionyl-	Coenzyme A-carboxylase (ATP-hydrolysing)]	ligase)	hypothetical protein MGC861	proteasome (prosome macropain) subunit beta	type 4	ESTs	ESTs	apolipoprotein A-I binding protein	kinase interacting with leukemia-associated	gene (stathmin)	cell division cycle associated 1	hypothetical protein MGC17528	hypothetical gene supported by BC007071	centromere protein F 350/400ka (mitosin)	chorionic somatomammotropin hormone 2	hypothetical protein FLJ22969	endothelial and smooth muscle cell-derived	neuropilin-like protein	SMC4 structural maintenance of	chromosomes 4-like 1 (yeast)	SMC4 structural maintenance of	chromosomes 4-like 1 (yeast)
NOLL	Hs.165909		Hs.87507	Hs.288549	Hs.36232	Hs.9329	Hs.93002	Hs.250822	Hs.79375		,	Hs.208912	Hs.89545		Hs.133294	Hs.133294	Hs.374850	Hs.127310		Hs.234545	Hs.300893	Hs.117305	Hs.77204	Hs.334372	Hs.146170	Hs.173374		Hs.50758	!	Hs.50758	
q21.31	q23.2		q23.3	q13.43	p11.21	q11.1	q13.12	q13.31	q22.13			q13.2	q21.2		q22	d22	d22	q23.2		q23.3	q24.3	q31.1	q32.3	q42.2	p21.32	q12.3		q26.1		q26.1	
17	17		17	19	20	20	20	20	7			22	<del>-</del>		_	~	~	~		₩.	<del></del>	<del>-</del>	<del></del>	_	က	က		က	(	က	
primary	primary		primary	primary	primary	primary	primary	primary	primary		,	primary	metastatic		metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	•	metastatic	
prostate	prostate		prostate	prostate	prostate	prostate	prostate	prostate	prostate			prostate	prostate		prostate	prostate	prostate	prostate		prostate	prostate	prostate	prostate	prostate	prostate	prostate		prostate	•	prostate	
L47276	BG165011		BF056791	AA719022	D80008	AF098158	U73379	AF011468	T77624			AI381686	AA630330		AW271106	AI690773	AI766666	AI249980		AI015982	H62656	N29457	U30872	AA151971	AI971357	W24316		AI338462	00000	AB019987	
681	<b>677</b>		675	682	989	685	688	687	701			689	723		771	773	803	739		798	745	753	96/	794	748	778		716	1,	/1/	
692	693		694	695	969	269	869	669	200		i	701	702		703	704	705	902		707	208	209	710	711	712	713		714	17	CL./	

									•																	
KIAA1363 protein	epithelial cell transforming sequence 2 oncogene	unknown	proteasome (prosome macropain) 26S subunit non-ATPase 2	heat shock 60kDa protein 1 (chaperonin)	unknown	thyroid hormone receptor interactor 13	cyclin B1	Homo sapiens cDNA FLJ11842 fis clone	HEMBA1006652 weakly similar to 60S RIBOSOMAL PROTEIN L7	anillin actin binding protein (scraps homolog	Drosophila)	hypothetical protein BC012331	replication protein A3 14kDa	paternally expressed 10	ESTs Highly similar to asparagine synthetase	[Homo sapiens] [H.sapiens]	polymerase (RNA) II (DNA directed)	polypeptide J 13.3kDa	riet proto-ortogene (riepatocyte grown ractor receptor)	ESTs Weakly similar to hypothetical protein	FLJ20378 [Homo sapiens] [H.sapiens]	exosome component Rrp41	nucleophosmin (nucleolar phosphoprotein B23 numatrin)		pituitary tumor-transforming 1	CGI-83 protein
Hs.22941	Hs.122579	NULL	Hs.74619	Hs.79037	NULL	Hs.6566	Hs.23960	Hs.374582		Hs.62180		Hs.87385	Hs.1608	Hs.137476	Hs.370106		Hs.80475	Hc 285754	13.2001.04	Hs.369347		Hs.343589	Hs.9614	Hs.283664	Hs.252587	Hs.118554
q26.32	q26.32	q26.33	d28	p14.3	p15.1	p15.33	q13.2	p21.1		p14.2		p15.3	p21.3	q21.3	q21.3		q22.1	23.4	4.	q33	;	NULL	q12.1	q12.3	q13.2	q13.3
က	က	က	က	2	S	ß	S.	ၑ		7		7	_	7	^		/	^	-	7	,	ω (	œ	ω (	∞ (	$\infty$
metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic		metastatic	metastatic	metastatic	metastatic		metastatic	metactatic	ווכומפומווכ	metastatic	;	metastatic	metastatic	metastatic	metastatic	metastatic
prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate		prostate		prostate	prostate	prostate	prostate		prostate	nroctata	בומוכסות	prostate	,	prostate	prostate	prostate	prostate	prostate
AL119157	BG170335	A1968388	AA194529	BE256479	AI750154	U96131	M25753	AI369840		AK023208		AI910524	L07493	AL582836	A1922470	!	L37127	AA103396		AI679933		AI571298	AA1915/6	AW001796	AA203476	AI525903
740	777	704	724	760	705	711	787	758		804		752	721	730	770	!	726	736	3	292	0	793	737	804	729	CR/
716	717	718	719	720	721	722	723	724		725		726	727	728	729	i	730	731	<u>.</u>	732	1	733	734	735	737	/3/

transcription elongation factor B (SIII)	DKFZP56400463 protein	collagen triple helix repeat containing 1	ESTs Moderately similar to leucine-rich neuronal protein [Homo sapiens] [H sapiens]	chronic myelogenous leukemia tumor antigen	mal T-cell differentiation protein 2	Homo sapiens mRNA cDNA DKFZp666E036	development and differentiation enhancing	factor 1	unknown	ZW10 interactor	cell division cycle 2 G1 to S and G2 to M	apoptosis-inducing factor (AIF)-homologous	mitochondrion-associated inducer of death	plasminogen activator urokinase	adenosine kinase	potassium large conductance calcium-	activated channel subfamily M alpha member	M-phase phosphoprotein 1	hypothetical protein FLJ10540	similar to RIKEN cDNA 2610036L13	FOS-like antigen 1	myeloma overexpressed gene (in a subset of	t(11 14) positive multiple myelomas)	Rac GTPase activating protein 1	rigognetical protein norm clone 645 Homo sapiens clone MGC:20874
Hs.184693	Hs.273344	Hs.283713	Hs.127286	Hs.195870	Hs.76550	Hs.356036	Hs.10669		NOLL	Hs.42650	Hs.334562	Hs.117062		Hs.77274	Hs.94382	Hs.89463		Hs.240	Hs.14559	Hs.23044	Hs.283565	Hs.116051		Hs.23900 Hs 206501	Hs.121973
q21.11	q22.3	q22.3	q23.1	q23.2	q24.12	q24.22	q24.22		q24.23	q21.1	q21.2	q22.1	,	q22.2	q22.2	q22.3		q23.31	q23.33	q13.1	q13.1	q13.3		q13.12	q13.12 q13.12
ω	∞	∞	ω	ω	∞	ω	ω		ω	9	9	10	:	9	10	9		10	9	7	7	7		<del>2</del> 5	7 2
metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	•	metastatic metastatic	metastatic
prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate		prostate	prostate	prostate	prostate	,	prostate	prostate	prostate		prostate	prostate	prostate	prostate	prostate	,	prostate prostate	prostate
AA995715	BE409290	AA584310	BF109660	AI802955	AL117612	AI880004	AI023398		AA527374	AF067656	AF154332	BC006121		K03226	U90339	AI198535		N27428	AI674163	BE614410	BG251266	AA621983		U82984 AF091087	A1936946
710	782	788	769	789	737	756	784		206	702	799	802		728	802	725		734	751	718	761	733	i	722 747	754
738	739	740	741	742	743	744	745		746	747	748	749	i	/20	751	752		753	754	755	756	757	1	759 759	760

Table 1 (Continued)

IMAGE:4547239 mRNA complete cds	UDP-N-acetyl-alpha-D- galactosamine:polypeptide N- acetylgalactosaminyltransferase 6 (GaINAc- T6)	keratin hair basic 1	extra spindle poles like 1 (S. cerevisiae)	polymerase (DNA directed) epsilon 2 (p59	Subdill()		hypothetical protein FLJ12618	nypometical protein FLJ10607 similar to	glucosamine-phosphate N-acetyltransferase	ERO1-like (S. cerevisiae)	Drosophila discs large-1 tumor supressor-like	cyclin-dependent kinase inhibitor 3 (CDK2-	associated dual specificity phosphatase)	ESTs Weakly similar to PSA3_HUMAN	Proteasome subunit alpha type 3 (Proteasome	component C8) (Macropain	methylenetetrahydrofolate dehydrogenase	(NADP+ dependent) methenyltetrahydrofolate	cyclohydrolase formyltetrahydrofolate	synthetase	MAD2 mitotic arrest deficient-like 1 (yeast)	p53-regulated DDA3	eukaryotic translation initiation factor 5	dynein cytoplasmic heavy polypeptide 1	cvclin-dependent kinase 2-interacting protein	CDC42 binding protein kinase beta (DMPK-	like)	hypothetical protein MGC13251
	Hs.151678	Hs.32952	Hs.153479	Hs.99185	Uc 274011	18.37.40.1	15.222021	18.2/821		Hs.25740	Hs.77695	Hs.84113		Hs.301231			Hs.172665				Hs.79078	Hs.77550	Hs.334810	Hs.7720	Hs.38205	Hs.12908		Hs.317821
	q13.13	q13.13	q13.13	q21.2	221.2		47 - 5 - 50 -	421.5		q21.3	q22.1	q22.1		q22.2			q23.1				q23.1	q32.12	q32.2	q32.2	q32.2	q32.2	-	q32.31
	7	12	12	4	7	† ×	<u> </u>	<u>+</u>		4	4	14		4			4				14	4	4	4	4	4		4
	metastatic	metastatic	metastatic	metastatic	motoctotic	motostatio	metastatic	וובומצומווכ		metastatic	metastatic	metastatic		metastatic			metastatic				metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic
	prostate	prostate	prostate	prostate	proctate	prostato	prostate	prostate		prostate	prostate	prostate		prostate			prostate				prostate	prostate	prostate	prostate	prostate	prostate	•	prostate
	AL118633	X81420	D79987	AF025840	A A 6.48033	DC006117	V10247014	10/1/07		AW268365	D13633	L25876		AI417084			J04031				<b>U65410</b>	AA926959	AL080102	BF000332	AI525727	AI761729		T65554
	707	741	762	727	744	740	7 10	2		21/9	780	785		992			735			,	738	731	764	779	786	800		746
	761	762	763	764	765	766	787	5		29	169	770		771			772				773	774	775	9//	777	778		779

Table 1 (Continued)

Homo sapiens clone MGC:16771 IMAGE:3907551 mRNA complete cds	cell division cycle associated 4	solute carrier family 16 (monocarboxylic acid transporters) member 3	ESTs	hypothetical protein PRO1855	ESTs	ESTs Weakly similar to hypothetical protein	FLJ20489 [Homo sapiens] [H.sapiens]	karyopherin alpha 2 (RAG cohort 1 importin	alpita 1)	thymidine kinase 1 soluble	signal recognition particle 68kDa	hematological and neurological expressed 1	ESTs	discs large (Drosophila) homolog-associated	protein 1	thymidylate synthetase	ubiquitin carrier protein	ubiquitin UBF-fl	chromosome 20 open reading frame 27	chromosome 20 open reading frame 139	serine/threonine kinase 6	solute carrier family 21 (organic anion	transporter) member 12	eukaryotic translation elongation factor 1 alpha	chromosome 21 open reading frame 45	WD repeat domain 4	Homo sapiens cDNA FLJ35467 fis clone	SMINT2005624
Hs.72363	Hs.34045	Hs.85838	Hs.201390	Hs.283558	Hs.298564	Hs.165909		Hs.159557		Hs.105097	Hs.273307	Hs.109706	Hs.127716	Hs.75814		Hs.82962	Hs.174070	Hs.288549	Hs.274422	Hs.135056	Hs.250822	Hs.235782		Hs.2642	Hs.49932	Hs. 143638	Hs.282961	
q32.31	q32.31	NOLL	NULL	q22	q22	q23.2		q24.3		q25.3	q25.3	q25.3	p11.22	p11.31		p11.32	q13.42	q13.43	p13	p13	q13.31	q13.33		q13.33	q22.11	q22.3	q22.3	
4	4	17	17	17	17	17		17		17	17	17	48	48		18	19	19	20	20	20	20		20	21	7	21	
metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic		metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	
prostate	prostate	prostate	prostate	prostate	prostate	prostate	•	prostate		prostate	prostate	prostate	prostate	prostate	•	prostate	prostate	prostate	prostate	prostate	prostate	prostate		prostate	prostate	prostate	prostate	
H04885	AI684508	U81800	AI292123	AI458014	AA564822	BG165011		U28386		K02581	AA312511	AI525822	AI733461	AB000277		X02308	M91670	AA719022	AI761506	H06350	AF011468	AW016409		X70940	AI652030	AI861913	AA577678	
755	797	715	774	743	775	767		742		713	719	759	772	783		712	209	208	792	793	720	714	•	765	791	703	757	
780	781	782	783	784	785	786		787		788	789	290	791	792		793	794	795	96/	797	798	799	) }	800	801	802	803	

Table 1 (Continued)

<b>(</b> e)		Protein	Protein	Protein	Protein	Protein	Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	Protein	Transcript	Transcript	Protein	Transcript	Transcript	Protein	Transcript	Transcript	Protein	Transcript	Transcript	Transcript
DNA segment on chromosome 21 (unique) 2056 expressed sequence	chromosome 21 open reading frame 70	unknown	unknown	unknown	unknown	unknown	unknown	unknown	unknown	unknown	unknown	unknown	unknown	unknown	ESTs	hypothetical protein FLJ36779	hypothetical protein FLJ36779	ESTs	hypothetical protein FLJ36779	hypothetical protein FLJ36779	ESTs	hypothetical protein FLJ36779	hypothetical protein FLJ36779	ESTs	hypothetical protein FLJ36779	hypothetical protein FLJ36779	Homo sapiens cDNA FLJ13017 fis, clone NT2RP3000628	Homo sapiens cDNA FLJ13017 fis, clone NT2RP3000628
Hs.110757	Hs.126522	NOLL	NOLL	NOLL	NOLL	NULL	NOLL	NOLL	NOLL	NOLL	NOLL	NOLL	NOLL	NOLL	Hs.196042	Hs.212613	Hs.212613	Hs.301858	Hs.301858									
q22.3	q22.3	q23.2	q23.2	q23.2	q23.2	q23.2	q23.2	q23.2	q23.2	q23.2	q23.2	q23.2	q23.2	p21.31	p24.3	q34.3	q34.3	p24.3	q34.3	q34.3	p24.3	q3 <b>4</b> .3	q34.3	p24.3	q34.3	q34.3	p31.3	p31.3
21	21	<del></del>	<del></del>	<del></del>	<del>-</del>	· -	<b>~</b>	~	<del>-</del> -	~	~	τ-	~	က	က	တ	တ	က	တ	တ	က	တ	တ	က	တ	တ	<del>-</del>	~
metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	primary	primary	primary	metastatic	metastatic	metastatic	primary	primary	primary	primary	primary
prostate	prostate	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	colon	colon	colon	colon	colon	colon	lung	lung
AI860822	A1983544	R62346	R62346	R62346	R62346	R62346	R62346	R62346	R62346	R62346	R62346	R62346	R62346	AA663786	AI962335	W25552	W25552	AI962335	W25552	W25552	A1962335	W25552	W25552	A1962335	W25552	W25552	AK022113	AK022113
781	790	120	120	120	120	120	120	120	120	120	120	120	120	197	194	227	227	11	101	101	334	393	393	301	328	328	527	527
804	805	908	807	808	808	810	811	812	813	814	815	816	817	818	819	820	821	822	823	824	825	826	827	828	829	830	831	832

Table 1 (Continued)

Protein	Transcript	Transcript		Transcript	Transcript		Protein		Transcript	Transcript	Protein	Protein	Protein	Protein	Protein	Transcript	Transcript	Protein	Transcript	Transcript
ESTs	ESTs	ESTs, Weakly similar to hypothetical	protein FLJ20837 [Homo sapiens] [H.sapiens]	ESTS	Homo sapiens cDNA FLJ14180 fis,	clone NT2RP2003799	Homo sapiens cDNA FLJ14180 fis,	Cione IN ZRPZ003/99	unknown	ESTs	hypothetical gene supported by BC007071									
Hs.125249	Hs.125249	Hs.144264		Hs.130107	Hs.296753		Hs.296753		NULL	Hs.373550	Hs.117305									
p15.1	p15.1	p13.2		g22.3	a21.11	-	q21.11		q13.3	p11.31	q31.1									
Ŋ	ນ	2		œ	∞		∞		ω	18	<del></del>	_	-	<del>-</del>	-	_	_	~	~	<b>—</b>
primary	primary	primary		primary	primary		primary		primary	primary	metastatic									
lung	oun	lung		hind	lung	n i	lung		lung		ø	prostate								
AA383208	AA383208	C00851		AA904882	AK024242		AK024242		AF232217	AI146765	N29457									
458	458	519		505	529		529		555	513	753	753	753	753	753	753	753	753	753	753
833	834	835		836	837	5	838		839	840	841	842	843	844	845	846	847	848	849	850

Table 1 (Continued)

Transcript	Transcript	Transcript	Transcript	Protein	Transcript	Protein	Protein		Protein		Protein0		Protein													
hypothetical gene supported by T BC007071	al gene supported by	al gene supported by	al gene supported by	unknown		Homo sapiens, clone MGC:16771		IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds
Hs.117305	Hs.117305	Hs.117305	Hs.117305	NULL	NOLL	Hs.72363	He 72363	13.7 2000	Hs.72363																	
q31.1	q31.1	q31.1	q31.1	p15.1	p15.1	q32.31	227 24	432.31	a32.31	-	q32.31	-	a32.31	-	q32.31	-	g32.31	-	a32.31	•	g32.31	-	q32.31	•	q32.31	-
~	~	<b>←</b>	~	rC	2	4	7	<u>t</u>	4	•	4		4		4		4		4		14		4		14	
metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	Cit Cit Cit	metastatic	metastatic		metastatic	ļ	metastatic													
prostate	prostate	prostate	prostate	nrostate	prostate	prostate	4.4	prostate	prostate																	
N29457	N29457	N29457	N29457	A1750154	AI750154	H04885		H04883	H04885		H04885	2	H04885		H04885		H04885		H04885		H04885	) ) -	H04885	) ) •	H04885	)
753	753	753	753	705	705	755	ı i	22	755	3	755	3	755	3	755	) }	755	}	755	3	755	)	755	)	755	) ) -
851	852	853	854	מהת	8 8 8 8 8 8	857	1	828	250	3	880	3	861	3	862	2	863	}	864	3	865	)	866	) )	867	;

# Table 1 (Continued)

Protein	Protein	Protein	Protein0	Protein	Protein	Protein	Protein	Protein	Drotein		Protein	Protein		Protein	Protein		Protein	Protein	: : : : :
	IMAGE:390/351, mRNA, complete cds Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds						-	IMAGE:3907551, mRNA, complete cds Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds Homo canions, clone MGC:16774	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771		IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds		IMAGE:3907551, mRNA, complete cds		IMAGE:3907551, mRNA, complete cds Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds
Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	He 70363	118.7.4.003	Hs.72363	Hs.72363		Hs.72363	Hs.72363		Hs.72363	Hs.72363	 
q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	432 34	456.5	q32.31	q32.31	0	q32.31	q32.31		q32.31	a32.31	
4	4	4	4	<del>4</del>	4	4	4	4	14	<u> </u>	4	4	•	4	14		4	4	
metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metactatic	ווכומאמווכ	metastatic	metastatic		metastatic	metastatic		metastatic	metastatic	
prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	nroefata	prostate	prostate	prostate	7 7	prostate	prostate		prostate	prostate	
H04885	H04885	H04885	H04885	H04885	H04885	H04885	H04885	H04885	HOARRS	200	H04885	H04885	100	H04885	H04885		H04885	H04885	
755	755	755	755	755	755	755	755	755	755	3	755	755	, ,	çç/	755		755	755	
898	869	870	871	872	873	874	875	876	877	5	878	879		088	881		882	883	

Table 1 (Continued)

Protein	Transcript	Protein	Protein	Transcript	Protein	Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	Franscript	Transcript	Franscript
Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Sb3		Homo sapiens, clone MGC:16771	8 8	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	cds	Spo	spo	· spo	<b>s</b> po	· spo	Spo	Sbo	spo	Homo sapiens, clone MGC:16771 TIMAGE:3907551, mRNA, complete cds
Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363
q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31
4	4	4	4	4	<del>4</del>	<del>4</del>	4	4	4	4	4	4	4	4	<del>4</del>
metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic
prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate
H04885	H04885	H04885	H04885	H04885	H04885	H04885	H04885	H04885	H04885	H04885	H04885	H04885	H04885	H04885	H04885
755	755	755	755	755	755	755	755	755	755	755	755	755	755	755	755
884	885	988	887	888	889	890	891	892	893	894	895	968	897	868	899

# Table 1 (Continued)

Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	Transcript
Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds		_			-						_	_			
Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363
q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31
4	<del>4</del>	4	4	4	4	4	4	4	4	<del>4</del>	<del>4</del>	4	4	4	4
metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic
prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate
H04885	H04885	H04885	H04885	H04885	H04885	H04885	H04885	H04885	H04885	H04885	H04885	H04885	H04885	H04885	H04885
755	755	755	755	755	755	755	755	755	755	755	755	755	755	755	755
006	901	902	903	904	902	906	206	806	606	910	911	912	913	914	915

Table 1 (Continued)

| Transcript                                                         |
|--------------------------------------------------------------------|--------------------------------------------------------------------|--------------------------------------------------------------------|--------------------------------------------------------------------|--------------------------------------------------------------------|--------------------------------------------------------------------|--------------------------------------------------------------------|--------------------------------------------------------------------|
| Homo sapiens, clone MGC:16771<br>IMAGE:3907551, mRNA, complete cds | Homo sapiens, clone MGC:16771<br>IMAGE:3907551, mRNA, complete cds | Homo sapiens, clone MGC:16771<br>IMAGE:3907551, mRNA, complete cds | Homo sapíens, clone MGC:16771<br>IMAGE:3907551, mRNA, complete cds | Homo sapiens, clone MGC:16771<br>IMAGE:3907551, mRNA, complete cds | Homo sapiens, clone MGC:16771<br>IMAGE:3907551, mRNA, complete cds | Homo sapiens, clone MGC:16771<br>IMAGE:3907551. mRNA. complete cds | Homo sapiens, clone MGC:16771<br>IMAGE:3907551, mRNA, complete cds |
| Hs.72363                                                           |
| q32.31                                                             | 14 q32.31                                                          |
| 4                                                                  | <del>4</del>                                                       | 4                                                                  | 4                                                                  | 4                                                                  | 4                                                                  | 4                                                                  | 4                                                                  |
| metastatic                                                         |
| prostate                                                           |
| H04885                                                             |
| 755                                                                | 755                                                                | 755                                                                | 755                                                                | 755                                                                | 755                                                                | 755                                                                | 755                                                                |
| 916                                                                | 917                                                                | 918                                                                | 919                                                                | 920                                                                | 921                                                                | 922                                                                | 923                                                                |

## WHAT IS CLAIMED IS:

1. A method for diagnosing cancer in a mammal, comprising determining amplification of a gene in the genome of a mammal wherein said gene is a gene of Table 1.

2. The method of claim 1 wherein said cancer is a member selected from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

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- 3. The method of claim 1 wherein said gene of Table 1 is a gene that encodes the same gene product as a polynucleotide selected from the polynucleotides of SEQ ID NO: 1 805 and 855 923.
- 4. The method of claim 1 wherein said mammal is a human patient.
  - 5. A method for diagnosing cancer or a pre-cancerous condition in a mammal, comprising:
  - (a) obtaining a cell or tissue sample from a mammal suspected of having cancer or a pre-cancerous condition and determining for said sample the gene copy number of a gene of Table 1;
    - (b) comparing said gene copy number of step (a) to the gene copy number of the same gene from a sample of a corresponding cell or tissue from a mammal of the same species not having cancer of the type being diagnosed

whereby a higher gene copy number determined in step (a) relative to that in step (b) indicates the presence of a cancer or pre-cancerous condition in the mammal of step (a) and results in a diagnosis of cancer or a pre-cancerous condition in said mammal.

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6. The method of claim 5 wherein said mammal is a human patient.

7. The method of claim 5 wherein said cancer is a member selected from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

- 8. The method of claim 5 wherein the gene of Table 1 is a gene that encodes the same gene product as a polynucleotide of SEQ ID NO: 1 805 and 855–923.
- A method of inhibiting cancer, or a pre-cancerous condition, in a
   mammalian cell, comprising contacting said cell with a molecule that inhibits function of a gene of Table 1.
  - 10. The method of claim 9 wherein said gene of Table 1 is a gene that encodes the same gene product as a polynucleotide of SEQ ID NO: 1 805 and 855 923.

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- 11. The method of claim 9 wherein said molecule inhibits gene function by binding to said gene.
- 12. The method of claim 9 wherein said molecule inhibits gene function by binding to an RNA encoded by said gene.
  - 13. The method of claim 9 wherein said molecule inhibits gene function by binding to polypeptide encoded by said gene.
  - 14. The method of claim 9 wherein said molecule is a member selected from an antisense DNA, an antisense RNA, a ribozyme and an siRNA.
- 15. The method of claim 9 wherein said cancer is a member selected 30 from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.
  - 16. The method of claim 9 wherein said contacting occurs in vivo.

17. A method for identifying an agent having therapeutic activity in a human patient in need of said therapeutic activity, comprising:

- (a) determining in a sample from a patient the level of a gene product encoded by a gene of Table 1 prior to administering a test compound to said patient;
  - (b) administering said test compound to said patient;
- (c) determining in a sample from said patient the level of a gene product encoded by the same the gene as in step (a)

wherein a decrease in the level of said gene product in step (c) relative to step (a) identifies said test compound as an agent having therapeutic activity.

- 18. The method of claim 17 wherein said therapeutic activity is anticancer activity.
  - 19. The method of claim 17 wherein said cancer is a member selected from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

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- 20. The method of claim 17 wherein said gene product is an RNA.
- 21. The method of claim 17 wherein said gene product is a polypeptide.

- 22. The method of claim 21 wherein said determination of said polypeptide is a determination of an enzyme activity.
- 23. The method of claim 17 wherein said gene of Table 1 is a gene that encodes the same gene product as a polynucleotide of SEQ ID NO: 1 805 and 855 923.

24. The method of claim 17 wherein said molecule is a member selected from an antisense DNA, an antisense RNA, a ribozyme and an siRNA.

- 5 25. A method for identifying an antineoplastic agent, comprising:
  - (a) contacting a test compound with a cell that expresses a gene of Table 1; and
  - (b) determining a change in gene expression as a result of said contacting;
- whereby said change in said gene expression identifies said test compound as an antineoplastic agent.
  - 26. The method of claim 25 wherein said change in expression is a decrease in expression.
    - 27. The method of claim 25 wherein said contacting occurs in vivo.

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- 28. The method of claim 25 wherein said gene of Table 1 encodes the same gene product as a polynucleotide of SEQ ID NO: 1 805 and 855 923.
- 29. The method of claim 25 wherein said molecule is a member selected from an antisense DNA, an antisense RNA, ribozyme, an siRNA, a small organic molecule and an antibody.
- 30. A method for determining the cancerous status of a cell, comprising determining elevated expression in said cell of a gene of Table 1 wherein elevated expression of said gene indicates that said cell is cancerous.
- 31. The method of claim 30 wherein said elevated expression is an elevated copy number of the gene.

32. The method of claim 30 wherein said gene of Table 1 encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 - 923.

- 33. A method for identifying a compound as an anti-neoplastic agent,comprising:
  - (a) contacting a test compound with a polypeptide encoded by a gene of Table 1,
  - (b) determining a change in a biological activity of said polypeptide due to said contacting,
- wherein a change in activity identifies said test compound as an agent having antineoplastic activity.

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- 34. The method of claim 33 wherein said gene of Table encodes the same gene product as a polynucleotide of SEQ ID NO: 1 805 and 855 923.
- 35. The method of claim 33 wherein said change in biological activity is a decrease in biological activity.
- 36. The method of claim 33 wherein said biological activity is an 20 enzyme activity.
  - 37. The method of claim 36 wherein said enzyme is selected from kinase, protease, peptidase, phosphodiesterase, phosphatase, dehydrogenase, reductase, carboxylase. transferase, deacetylase and polymerase.
    - 38. The method of claim 37 wherein said kinase is a protein kinase.
- 39. The method of claim 37 wherein said kinase is a serine or 30 threonine kinase.

40. The method of claim 37 wherein said kinase is a receptor tyrosine protein kinase.

- 41. The method of claim 37 wherein said protease is a serine protease, cysteine protease or aspartic acid protease.
  - 42. The method of claim 37 wherein said transferase is a methyltransferase.
- 10 43. The method of claim 42 wherein said methyl transferase is a cytidine methyltransferase or an adenine methyltransferase.

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- 44. The method of claim 37 wherein said deacetylase is a histone deacetylase.
- 45. The method of claim 37 wherein said carboxylase is a  $\gamma$ -carboxylase.
- 46. The method of claim 37 wherein said peptidase is a zinc peptidase.
  - 47. The method of claim 37 wherein said polymerase is a DNA polymerase.
- 48. The method of claim 37 wherein said polymerase is a RNA polymerase.
  - 49. The method of claim 33 wherein said biological activity is a membrane transport activity.
- 30 50. The method of claim 33 wherein said polypeptide is a cation channel protein, an anion channel protein, a gated-ion channel protein or an ABC transporter protein.

51. The method of claim 33 wherein said polypeptide is an integrin.

52. The method of claim 33 wherein said polypeptide is a Cytochrome P450 enzyme.

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- 53. The method of claim 33 wherein said polypeptide is a nuclear hormone receptor.
- 54. The method of claim 33 wherein said biological activity is a receptoractivity.
  - 55. The method of claim 33 wherein said receptor is a G-protein-coupled receptor.
- 15 56. The method of claim 33 wherein said polypeptide is contained in a cell.
  - 57. The method of claim 33 wherein said molecule is a member selected from antisense DNA, an antisense RNA, a ribozyme, an siRNA, a small organic molecule and an antibody.
  - 58. The method of claim 57 wherein said antibody is specific for a polypeptide comprising an amino acid sequence of SEQ ID NO: 806 854.
- 59. A method for identifying an anti-neoplastic agent comprising contacting a cancerous cell with a compound found to have anti-neoplastic activity in the method of claim 59 under conditions promoting the growth of said cell and detecting a change in the activity of said cancerous cell.
- 30 60. The method of claim 59 wherein said change in activity is a decrease in the rate of replication of said cancerous cell.

61. The method of claim 59 wherein said change in activity is the death of said cancerous cell.

- 62. A method for treating cancer comprising contacting a cancerous cell with an agent first identified as having gene modulating activity using the method of claim 25, 33, or 59 and in an amount effective to cause a reduction in cancerous activity of said cell.
- 63. The method of claim 62 wherein said cancerous cell is contacted *in* 10 *vivo*.
  - 64. The method of claim 62 wherein said reduction in cancerous activity is a decrease in the rate of proliferation of said cancerous cell.
- 15 65. The method of claim 62 wherein said reduction in cancerous activity is the death of said cancerous cell.
- 66. The method of claim 62 wherein said cancer is a member selected from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.
  - 67. A method for treating cancer comprising contacting a cancerous cell with an agent having affinity for an expression product of a gene of Table 1 and in an amount effective to cause a reduction in cancerous activity of said cell.

- 68. The method of claim 67 wherein said expression product is a polypeptide.
- 30 69. The method of claim 67 wherein said molecule is a member selected from antisense DNA, an antisense RNA, a ribozyme, an siRNA, a small organic molecule and an antibody.

70. The method of claim 69 wherein said antibody is specific for a polypeptide comprising an amino acid sequence selected from SEQ ID NO: 806-854.

- 5 71. A method for monitoring the progress of cancer therapy in a patient comprising monitoring in a patient undergoing cancer therapy the expression of a gene of Table 1.
- 72. The method of claim 71 wherein said gene encodes the same gene product as a polynucleotide of SEQ ID NO: 1 805 and 855 923.
  - 73. The method of claim 71 wherein said cancer therapy is chemotherapy.
- 15 74. The method of claim 71 wherein said cancer is a member selected from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.
- 75. A method for determining the likelihood of success of cancer therapy in a patient, comprising monitoring in a patient undergoing cancer therapy the expression of a gene of Table 1 wherein a decrease in said expression prior to completion of said cancer therapy is indicative of a likelihood of success of said cancer therapy.
- 25 76. The method of claim 75 wherein said gene encodes the same gene product as a polynucleotide of SEQ ID NO: 1 805 and 855 923.
  - 77. The method of claim 75 wherein said cancer therapy is chemotherapy.

78. The method of claim 744 wherein said cancer is a member selected from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

- 79. A method for producing test data with respect to the anti-neoplastic activity of a compound comprising:
  - (a) identifying a test compound as having anti-neoplastic activity using a method of claim 25;
  - (b) producing test data with respect to the anti-neoplastic activity of said test compound sufficient to identify the chemical structure of said test compound.
  - 80. A method for producing test data with respect to the anti-neoplastic activity of a compound comprising:
- (a) identifying a test compound as having anti-neoplastic activity usinga method of claim 33;
  - (b) producing test data with respect to the anti-neoplastic activity of said test compound sufficient to identify the chemical structure of said test compound.
- 20 81. A method for determining the progress of a treatment for cancer in a patient afflicted therewith, following commencement of a cancer treatment on said patient, comprising:
  - (a) determining in said patient a change in expression of one or more genes of Table 1; and
  - (b) determining a change in expression of said gene compared to expression of said one or more determined genes prior to said cancer treatment;

wherein said change in expression indicates progress of said treatment thereby determining the progress of said treatment.

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82. The method of claim 81 wherein said change in expression is a decrease in expression and said decrease indicates success of said treatment.

5 83. The method of claim 81 wherein said gene encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 - 923.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: DETERMINING CANCER-LINKED GENES AND THERAPEUTIC TARGETS USING MOLECULAR CYTOGENETIC METHODS

(57) Abstract: Methods for identifying potential therapeutic agents, such as anti-tumor agents, based on their modulation of the expression of specified genes, especially genes mapping to specific chromosomal regions, are disclosed. Also described are methods for diagnosing cancerous, or potentially cancerous, conditions as a result of the expression, or patterns of expression, of such genes, including detecting changes in levels of gene copy number and/or level of amplification of the said gene, or sets of genes, to detect and/or diagnose the cancer. Methods for detecting or determining functionally related genes, as well as methods for treating cancer based on targeting expression products of such genes, determining genes involved in the cancerous process and the success and/or response rates and survival statistics for cancer patients on treatment are encompassed by the invention. Also encompassed are methods involving determining the modulated expression of the genes in these regions of interest (ROIs) as pharmacodynamic/pharmacogenetic/surrogate markers and/or for patient profiling prior to accrual for clinical trials/treatments based on the identification of these genes as validated gene/drug targets in various cancer tissue types.



# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/09289

A. CLASSIFICATION OF SUBJECT MATTER IPC(7) : C12Q 1/68	
US CL : 435/6	
According to International Patent Classification (IPC) or to both na	tional classification and IPC
B. FIELDS SEARCHED	
Minimum documentation searched (classification system followed b U.S.: 435/6	y classification symbols)
Documentation searched other than minimum documentation to the	extent that such documents are included in the fields searched
Electronic data base consulted during the international search (name Please See Continuation Sheet	e of data base and, where practicable, search terms used)
C. DOCUMENTS CONSIDERED TO BE RELEVANT	
Category * Citation of document, with indication, where a	
X WO 01/92581 A2 (CORIXA CORPORATION) 06 I NO:8806, 8674, 8852, 8742, 8737, 8984, and pages	December 2001 (06.12.2001), SEQ ID 1-83 360-448.
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Further documents are listed in the continuation of Box C.	See patent family annex.
Special categories of cited documents:	"T" later document published after the international filing date or priority
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Date of the actual completion of the international search	Date of mailing of the international search report  24 FEB 2095
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# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/09289

$Box\ No.\ II \qquad Observations\ where\ certain\ claims\ were\ found\ unsearchable\ (Continuation\ of\ item\ 2\ of\ \ first\ sheet)$
This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2. Claims Nos.:  because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. Claims Nos.:  because they are dependent claims and are not drafted, in accordance with the second and third sentences of Rule 6.4(a).
Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows: Please See Continuation Sheet
<ol> <li>As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.</li> <li>As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.</li> <li>As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:</li> </ol>
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-83 (partial) regarding SEQ ID NO:1
Remark on Protest The additional search fees were accompanied by the applicant's protest.
No protest accompanied the navment of additional search fees  Form PCT/ISA/210 (continuation of first cheet/2)) (Innuary 2004)

Form PCT/ISA/210 (continuation of first sheet(2)) (January 2004)

INTERNATIONAL SEARCH REPORT	International application No. PCT/US04/09289
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BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACK. This application contains the following inventions or groups of inventions which are concept under PCT Rule 13.1. In order for all inventions to be examined, the appr	e not so linked as to form a single general inventive
Group 1, claim(s) 1-83 (partial), drawn to methods of diagnosing cancer relating to	SEQ ID NO:1.
Groups 2-874, claim(s) 1-83 (partial), drawn to methods of diagnosing cancer relat	ing to SEQ ID NO:2-805 and 855-923, respectively.
The inventions listed as Groups 1-874 do not relate to a single general inventive co 13.2, they lack the same or corresponding special technical features for the following a structure which is not shared with any of the other nucleic acids; thus, the structure of the nucleic acid, defined by its nucleotide sequence. So there is no condifferent Groups.	ng reasons: each of the groups relates to a nucleic acid special technical feature of each Group is the
Continuation of B. FIELDS SEARCHED Item 3: USPAT, PGPUB, DERWENT WPI, MEDLINE, BIOSIS, GENEMBL, GENESE search terms: cDNA, gene, cancer, SEQ ID NO:1	Q
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